PROMOTION RECOMMENDATION The University of Michigan School of Public Health Department of Biostatistics

Xiang Zhou, assistant professor of biostatistics, Department of Biostatistics, School of Public Health, is recommended for promotion to associate professor of biostatistics, with tenure, Department of Biostatistics, School of Public Health.

Academic	Degrees:

Ph.D.	2010	Duke University, Neurobiology, Durham, NC
M.S.	2009	Duke University, Statistics, Durham, NC
B.S.	2004	Peking University, Biology, Beijing, China

Professional Record:

2018-present	John G. Searle Assistant Professor of Biostatistics, University of Michigan
2014-present	Assistant Professor, Department of Biostatistics, University of Michigan
2013-2014	William H. Kruskal Instructor, Department of Statistics, University of Chicago
2010-2013	Post-doctoral Scholar, Department of Human Genetics, University of Chicago

Summary of Evaluation:

<u>Teaching</u>: Professor Zhou is a committed and talented teacher who has taught some of the key and most challenging courses in our portfolio, with excellent to outstanding evaluations. Highlights in his diverse teaching portfolio include courses on probability and distribution theory (BIOSTAT 601); on longitudinal analysis (BIOSTAT 653); on statistical models and numerical methods in human genetics (BIOSTAT 666); and special topics in modern statistical computing (BIOSTAT 830). His effort to redesign the traditional longitudinal data analysis course BIOSTAT 653 to make it more relevant for current problems and advance students understanding of the subject matter is particularly noteworthy. He is a key instructor in our computational courses and a very important source of consultation in scalable computation for students and colleagues in the department. He is playing a critical role in developing the health data science concentration.

Professor Zhou has been active in doctoral student advising and is presently supervising six doctoral students. He is also serving as a mentor of two post-doctoral fellows. He has been active in mentoring visiting students and scholars. He is currently supporting five doctoral students on his research and collaborative grants.

<u>Research:</u> Professor Zhou is an outstanding data scientist focused on developing statistical and computational methods for genetic and genomic studies. These often include large-scale multiplatform "omics" data including genome-wide association studies of single nucleotide polymorphisms, epigenetic studies of DNA methylation and functional genomic sequencing studies leading to RNAseq and ChIPseq data. By developing novel analytic methods to efficiently extract information from these high-dimensional heterogeneous data sources, Professor Zhou has advanced our understanding of the genetic basis of phenotypic variation for human diseases and disease related quantitative traits. His research has appeared in high-impact journals in *Biostatistics, Bioinformatics, Genetics,* and *Computational Biology*. Professor Zhou's research is supported by strong extramural funding from a diverse body of funding agencies including the NIH, the NSF and the Chan-Zuckerberg Initiative.

Professor Zhou works in the burgeoning field of statistics that seeks to develop and apply innovative, flexible, scalable and efficient computational and inferential methods for dealing with large multiplatform genomics data, particularly the data that arise from modern biological experiments. His body of work on gene mapping of complex traits using a mixed model variance-component framework has led to a collection of landmark papers in the field. Together, this relatively recent body of papers has been cited more than 2,400 times.

Professor Zhou is best known for two series of important contributions. In one line of work he has developed variance component methods for investigating polygenic contributions to complex traits. The method proposed by Professor Zhou and his colleagues using Bayesian sparse linear mixed models (implemented in a widely popular software *GEMMA*) is routinely used by many researchers worldwide. His recent paper on estimating variance components in linear mixed models using only summary statistics is viewed as a seminal contribution to this field and is already widely used. In recent extensions of this work, Professor Zhou has integrated functional information from databases like GTeX and ENCODE to bolster the power of gene-mapping within a mixed model framework. This work has led to general foundational work in the area of Bayesian variable selection and shrinkage. He has been a true pioneer in heritability estimation of complex traits.

In a second line of work, Professor Zhou has proposed methods for joint analysis of diverse data types: analyzing differential DNA methylation using bisulfite sequencing data, methods for detecting epistasis and analysis of gene-environment interactions. Methods and ideas developed by Professor Zhou are used in the analysis of many modern studies and have also served as the foundation for further methods development by others. He has recently begun his collaboration in large-scale studies like TOPMED, GENOA and MESA at the University of Michigan in the areas of association, interaction and mediation with high dimensional genomic data.

Professor Zhou has 43 published/in press articles (including 25 as first, co-first and/or corresponding/co-corresponding author). Among these 43 articles, about one half are in absolutely top journals (*Nature Genetics, Nature Communications, PloS Genetics, Bioinformatics, Journal of the American Statistical Association, The Annals of Applied Statistics, The American Journal of Human Genetics, Genome Biology, PNAS*). Twenty-seven of these 43 papers have already received >10 citations and five of them have more than 100 citations. These include both methodological papers and applied collaborations. This showcases the breadth and depth of Professor Zhou's most influential work, cutting across important and diverse fields in science. This high-quality publication record is impressive for a junior scholar at his level. As a testament to his prolific research, Professor Zhou has received substantial research funding as a PI including three R01's, a NSF methodology award and an award from the Chan-Zuckerberg initiative.

Recent and Significant Publications:

- Xiang Zhou (2017). A unified framework for variance component estimation with summary statistics in genome-wide association studies. *Annals of Applied Statistics*. 11: 2027-2051.
- Lorin Crawford, Ping Zeng, Sayan Mukherjee, and Xiang Zhou (2017). Detecting epistasis with the marginal epistasis test in genetic mapping studies of quantitative traits. *PLoS Genetics*. 13(7):e1006869.
- Ping Zeng and Xiang Zhou (2017). Nonparametric genetic prediction of complex traits with latent Dirichlet process regression models. *Nature Communications*. 8(1):456.
- Xingjie Hao,Ping Zeng, Shujun Zhang, and Xiang Zhou (2018). Identifying and exploiting traitrelevant tissues with multiple functional annotations in genome-wide association studies. *PLoS Genetics.* 14(1):e1007186.

Mengjie Chen and Xiang Zhou (2018). Variability-preserving imputation for accurate gene expression recovery in single cell RNA sequencing studies. *Genome Biology*. 19(1):196.

<u>Service:</u> Professor Zhou is a generous and thoughtful contributor to departmental life and committees. He is a regular contributor to faculty meetings and discussions. He has been an active member in a variety of key committees, including the biostatistics curriculum committee (which meets regularly to define and discuss the graduate program in biostatistics and our offerings to non-majors), admission committee (which reviews hundreds of applicants for our highly selective doctoral and masters program), candidacy committee (which manages and grades the annual qualifying exam and other course requirements for doctoral students). These three committees have substantial workloads.

Professor Zhou is a good citizen of the broader genomics community beyond the department. He has organized the Genome Science Training Program (GSTP) seminar series for three consecutive years and is the current organizer of the Center for Statistical Genetics (CSG) journal club. He is integral to the thriving statistical genetics and genomics research community at University of Michigan.

Professor Zhou has moderated sessions for several national and international conferences, such as the Annual Meeting of the American Society for Human Genetics (ASHG, 2017) and the Midwest Statistics Conference for which he also served as a principal organizer. In addition to these roles, he is a regular reviewer for several top journals both in the areas of biostatistics and statistical genetics and genomics and reviews 12-18 papers per year. Professor Zhou has served as a guest editor for *PLoS Genetics* and *PLoS Computational Biology* and as a grant reviewer for the Medical Research Council, UK.

External Reviewers:

Reviewer A: "I find his track record of external funding support to be outstanding and far ahead of other investigators at a similar stage of career. ... Dr. Zhou is clearly on a path to become one of the leaders in the field of statistical genetics. ... Given his outstanding track records in grant support, publications, and teaching, I recommend Dr. Zhou's promotion to Associate Professor with Tenure without hesitation. He clearly is a superstar in the making."

Reviewer B: "In his research, he develops novel computational and statistical methodology that are motivated and address current important problems in the field. His work is highly creative and the range of problems that he works in is quite broad."

Reviewer C: "In summary, Xiang has done outstanding research work in our field, and complements very well the statistical genetics group in Michigan. I strongly believe that he is one of the most promising young statistical geneticists..."

Reviewer D: "It is very impressive what Dr. Zhou has accomplished in only 4 years as a faculty member at the University of Michigan, and I think he really stands out in his peer group."

Reviewer E: "A constant of Zhou's work is the care with which he makes available software that implements the methods he develops: this is an important requirement of reproducibility, but, most fundamentally, the vehicle by which his work is most likely to be impactful in science. ... I find that Zhou;s research activity is vibrant and diverse: his contributions are numerous, on timely topics, and showcase a sensitivity to the computational challenges presented by large scale biomedical data that insure their relevance."

Reviewer F: "Quite simply, Dr. Zhou is a star in the field of statistical genetics. ... I cannot give Dr. Zhou a stronger recommendation to appointment as Associate Professor with tenure at your prestigious institution."

Reviewer G: "I can say that this is the strongest case for promotion and tenure I have seen in quite some time."

Reviewer H: "His productivity over the past 4 years has been truly remarkable, and he has clearly established himself as a highly respected independent researcher and one of the leading statistical geneticists in the field."

Summary of Recommendation:

Professor Zhou is a prolific biostatistician of the highest caliber and fully deserving of promotion and tenure. He has made profound and often pioneering contributions to methodology for gene-mapping and heritability estimation of complex traits using linear mixed models. He has engaged in varied and fruitful collaboration with researchers across campus and elsewhere. Professor Zhou is an outstanding teacher, mentor and is very active and engaged in the departmental mission and service. He certainly stands out as a leader in his peer group at any premier institution. It is with the support of the School of Public Health Executive Committee that I recommend Xiang Zhou for promotion to associate professor of biostatistics, with tenure, Department of Biostatistics, School of Public Health.

F. DuBois Bowman, Ph.D. Dean, School of Public Health

May 2019