

Sebastian Zöllner  
Searle Assistant Professor of Biostatistics,  
Assistant Professor of Psychiatry  
1420 Washington Heights M4610  
Ann Arbor Michigan 48109  
734 647 9465  
szoellne@umich.edu

## Education and Training History

- 9/90 – 4/97      Diploma degree (M. Sc.) in Mathematics, University of Munich, Germany.
- 6/97 – 4/01      Ph. D. in Biological Sciences, University of Munich/Max-Planck Institute for Evolutionary Anthropology, Leipzig, Germany  
Adviser: Arndt von Haeseler
- 4/01-11/01      Post Doctoral Fellow, Max-Planck Institute for Evolutionary Anthropology, Leipzig, Germany
- 12/01–7/05      Post Doctoral Fellow, Department of Human Genetics, University of Chicago  
Adviser: Jonathan Pritchard

## Academic Appointments

- 8/05 –            Assistant Professor, Departments of Biostatistics and Psychiatry, University of Michigan.

## Research Interests

**Population Genetics:** Human genome variation provides intriguing insights into the evolution of our species and into the biology of heritable traits. My research focuses on developing methods for modeling the stochastic processes generating this variation. Based on these models I make inferences about human population history and develop tools for mapping disease variants.

**Copy number variation:** Copy number variants (CNVs) are segments of the genome that exist in different copy numbers in the population. As CNVs encompass genes as well as non-coding DNA, they are good candidates for functional variation. I have design methods for competitive genome hybridization (CGH) data and for hybridization intensities in SNP genotype data.

**Rare Variants:** As it is now possible to generate extensive sequence data for large samples, it may be possible to understand the contribution of rare variants to common complex diseases. I am working on several approaches to address statistical challenges related to this new data.

**Genetics of psychiatric diseases:** Most psychiatric diseases have high heritability; for example bipolar disorder has a sibling relative risk of 8. Nevertheless, identifying risk variants affecting these diseases has been challenging. I address this challenge by applying modern genetic tools and developing methods to understand the phenotypic heterogeneity of many disorders.

## Honors and Awards

- 2002        Katz Postdoctoral Fellowship, University of Chicago  
2006        Rachel Upjohn Clinical Scholar Award, University of Michigan  
2009        John G Searle Assistant Professor of Biostatistics, University of Michigan

## Membership in Professional Societies

American Society of Human Genetics  
American Statistical Association

## Bibliography

### *Peer-reviewed papers*

1. Terwilliger J, Zöllner S, Laan M, Pääbo S. Mapping genes through the use of linkage disequilibrium generated by genetic drift: 'Drift Mapping' in small populations with no demographic expansion. *Hum Hered* 48:138-154, 1998.
2. Zöllner S, von Haeseler A. A coalescent approach to study linkage disequilibrium between single nucleotide polymorphisms *Am J Hum Genet* 66:615-628, 2000.
3. Kaessmann H\*, Zöllner S\*, Gustafsson AC, Wiebe V, Laan M, Lundeberg J, Uhlén, Pääbo S. Extensive linkage disequilibrium in small human populations in Eurasia. *Am J Hum Genet* 70:673-685, 2002; \* denotes equal contribution.
4. Enard W, Khaitovich P, Klose J, Zöllner S, Heissig F, Giavalisco P, Nieselt-Struwe K, Muchmore E, Varki A, Ravid R, Doxiadis GM, Bontrop RE, Pääbo S. Intra- and interspecific variation in primate gene expression patterns. *Science* 296: 340-343, 2002.
5. Kaessmann H, Zöllner S, Nekrutenu A, Li HW. Signatures of domain shuffling in the human genome. *Genome Res* 12: 1642-1650, 2002.
6. Hellmann I, Zöllner S, Enard W, Ebersberger I, Nickel B, Pääbo S. Selection on human genes as revealed by comparison to chimpanzee DNA. *Genome Res* 13: 831-837, 2003.
7. Zöllner S, Wen X, Hanchard N, Herbert M, Ober C Pritchard J. Evidence for extensive transmission distortion in the human genome *Am. J. Hum. Genet.* 70:673-685, 2004.
8. Zöllner S, Pritchard JK. A coalescent based approach for disease mapping. *Lecture Notes in Bioinformatics: Computational methods for SNPs and haplotype inference*, 2983:124–130, 2004.
9. Zöllner S, Pritchard J. Coalescent-based association mapping and fine mapping of complex trait loci. *Genetics* 169: 1071-1092, 2005.
10. Zöllner S, Wen X, Pritchard JK. Association mapping and fine mapping with TreeLD. *Bioinformatics* 21: 3168-3170, 2005.

11. Zöllner S, Pritchard JK. Overcoming the winner's curse: estimating penetrance parameters from case-control data. *Am J Hum Genet* 80: 605-615, 2007.
12. Liang L, Zöllner S, Abecasis GR. GENOME: a rapid coalescent-based whole genome simulator. *Bioinformatics* 23:1565-1567, 2007.
13. Zandi PP, Zöllner S, Avramopoulos D, Willour VL, Qin ZS, Burmeister M, Miao K, Gopalakrishnan S, Potash JB, DePaulo JR, McInnis MG. Family – based SNP association study on 8q24 in bipolar disorder. *Am J Med Genet B Neuropsychiatr Genet.* 147B(5): 612-618, 2008.
14. Burmeister M, McInnis MG, Zöllner S. Psychiatric genetics: progress among controversies. *Nat Rev Genet* 9: 527-540, 2008.
15. She X, Cheng Z, Zöllner S, Church D, Eichler EE. Extensive copy number variation of mouse segmental duplications. *Nat Genet* 40: 909-914, 2008.
16. Zhang D, Cheng L, Qian Y, Alliey-Rodriguez N, Kelsoe JR, Greenwood T, Nievergelt C, Barrett TB, McKinney R, Schork N, Smith EN, Bloss C, Nurnberger J, Edenberg HJ, Foroud T, Sheftner W, Lawson WB, Nwulia EA, Hipolito M, Coryell W, Rice J, Byerley W, McMahon F, Schulze TG, Berrettini W, Potash JB, Belmonte PL, Zandi PP, McInnis MG, Zöllner S, Craig D, Szelinger S, Koller D, Christian SL, Liu C, Gershon ES. Singleton deletions throughout the genome increase risk of bipolar disorder. *Mol Psychiatry* 14: 376-380, 2009.
17. Zöllner S, Su G, Stewart WC, Chen Y, McInnis MG, Burmeister M. EM Algorithm for scoring polymorphic deletions from SNP data and application to a common CNV on 8q24. *Genet Epidemiol* 33: 357-368, 2009.
18. Henrichsen CN\*, Vinckenbosch N\*, Zöllner S\*, Chaignat E, Pradervand S, Ruedi M, Kaessmann H, Reymond. Segmental copy number variation shapes tissue transcriptomes. *Nat Genet* 41: 424-429, 2009; \* denotes equal contribution
19. Saunders EF, Zhang P, Copeland JN, McInnis MG, Zöllner S. Suggestive linkage at 9p22 in bipolar disorder weighted by alcohol abuse. *Am J Med Genet B Neuropsychiatr Genet.* 150B: 1133-8, 2009.
20. Smith EN, Bloss CS, Badner JA, Barrett T, Belmonte PL, Berrettini W, Byerley W, William Coryell W, Craig D, Edenberg HJ, Eskin E, Foroud T, Gershon E, Greenwood TA, Hipolito M, Koller DL, Lawson WB, Liu C, Lohoff F, McInnis MG, McMahon FJ, Mirel DB, Murray SS, Nievergelt C, Nurnberger J, Nwulia EA, Paschall J, Potash JB, Rice J, Schulze TG, Scheftner W, Panganiban C, Zaitlen N, Zandi PP, Zöllner S, Schork NJ, Kelsoe JR. Genome-wide association study of bipolar disorder in European American and African American individuals. *Mol Psychiatry* 14: 755-63, 2009

21. Zöllner S, Teslovich TM. Using GWAS data to identify copy number variants contributing to common complex diseases. *Statistical Science* 24: 530-46, 2009

### ***Book chapters***

1. Zöllner S, von Haeseler A. History and Linkage Disequilibrium. *Encyclopedia of Life Sciences*, Nature Publishing Group, London 2002. (peer-reviewed)
2. Zöllner S. Population History and Linkage Disequilibrium. *Encyclopedia of Life Sciences*, John Wiley & Sons, Ltd, 2008. (peer-reviewed)

### ***Manuscripts submitted for publication***

1. Zhang P, Xiang N, Silwerska E, Chen Y, McInnis MG, Burmeister M, Zöllner S. Family-based association analysis using over 2500 SNPs to finemap bipolar linkage peak on chromosome 8q24.
2. Zawistowski M, Gopalakrishnan S, Li Y, Zöllner S. Extending rare variant testing strategies: analysis of non-coding sequence and imputed genotypes.
3. Zöllner S. CopyMap: Localization and calling of copy number variation by joint population analysis of oligonucleotide and competitive genomic hybridization data.

### ***Manuscripts in preparation***

1. Smith EN, Koller DL, Pannigan C, Szelinger S, Zhang P, Badner JA, Barrett T, Belmonte PL, Berrettini W, Bloss CS, Byerley W, Coryell W, Edenberg HJ, Foroud T, Gershon E, Greenwood TA, Hipolito M, Lawson WB, Liu C, Lohoff F, McInnis MG, McMahon FJ, McKinney R, Murray SS, Nievergelt C, Nurnberger J, Nwulia EA, Potash JB, Rice J, Schulze TG, Scheftner W, Zandi PP, Zöllner S, Craig D, Schork NJ, Kelsoe JR. Genome-wide association of bipolar disorder suggests an enrichment of functional variants in regions near exons.
2. Gopalakrishnan S, Zöllner S. Admixture mapping under a rare variant paradigm.
3. Zawistowski, M., Gopalakrishnan, S., and Zöllner, S. Imputation strategies for rare variants.

## **Invited Extramural Presentations**

- 2000 · Tenth conference on mathematical and statistical aspects of molecular biology, Cambridge, UK
- 2001 · IZKF Summer School, Grossbooten, Germany
- 2002 · 5<sup>th</sup> International meeting on SNPs and complex genome analysis, Reykjavik, Island

- Department of Genetics, Max-Planck Institute for Evolutionary Anthropology, Leipzig, Germany
- 2003
  - Workshop on medical statistics, Oberwolfach, Germany
  - Department of Bioinformatics, University of Düsseldorf, Germany
  - BSD Retreat, Eagle Ridge, USA
- 2004
  - Workshop on Bioinformatics, Vienna
  - Division of Human Cancer Genetics, Ohio State University
- 2005
  - Southwestern University, Dallas
  - New York University, New York
  - University of Washington, Seattle
  - American Society of Human Genetics Annual Meeting, Park City
- 2006
  - Conference on Psychiatric Genetics, Salt Lake City
  - Pennsylvania State University, State College
  - Institute Gulbenkian de Cien, Portugal
- 2007
  - Conference on Psychiatric Genetics, Park City
  - American Society of Human Genetics Annual Meeting, San Diego
  - Universität Regensburg, Germany
  - Department of Biology, Ludwigs-Maximilians Universität München, Germany
- 2008
  - Conference on Psychiatric Genetics, Park City
  - Department of Epidemiology, Ludwigs-Maximilians Universität München, Germany
  - Investigator meeting GxE interaction, Bethesda
- 2009
  - Conference on Psychiatric Genetics, Park City
  - Investigator meeting GxE interaction, Bethesda
  - Joint statistical meeting, Washington
- 2010
  - Meeting of the India Statistical Society, Vizak, India
  - GSK resequencing workshop
  - Investigator meeting GxE interaction, Bethesda
  - ENAR Spring Meeting, New Orleans

## **Teaching**

### ***Supervised Undergraduate Students***

Rui Zhao (Statistics) 2008

### ***Supervised Graduate Students***

Yi Chen (Biostatistics) 2005-2007

Peng Zhang (Biostatistics) 2007 – 2009

Peng Zhang (Bioinformatics) 2009-

Kraig Stevenson (Biostatistics) 2007-2009

Mathew Zawistowski (Biostatistics) 2007-

Syam Gopalakrishnan (Biostatistics) 2008-  
Ziqian Geng (Biostatistics) 2009-  
Dan Maixner (OJOC) 2008-2009

### ***Pre-Thesis Committees***

Jenna van Liere (Bioinformatics) 2007  
Michael DeGiorgio (Bioinformatics) 2008  
Jennifer Smith (Epidemiology) 2008  
Lucy Huang (Biostatistics) 2009 (Chair)  
Erika Flannery (Epidemiology) 2009  
Chaolong Wang (Bioinformatics) 2010 (Chair)

### ***Dissertation Committees***

Karen Coneely (Biostatistics) 2006 - 2007  
Riu Xiao (Biostatistics) 2006-2009  
Liming Liang (Biostatistics) 2008-2009  
Jenna van Liere (Bioinformatics) 2007-2008  
Chris van Hout (Human Genetics) 2007 -  
Nicole Scott (Human Genetics) 2007 – 2010  
Michael DeGiorgio (Bioinformatics) 2009 –  
Lucy Huang (Bioinformatics) 2009 -  
Erika Flannery (Epidemiology) 2009 -  
Jennifer Smith (Epidemiology) 2008 -  
Huateng Huang (Ecology and Evolutionary Biology) 2010-

### ***Formal Courses***

1997 – 1998	Teaching assistant for ‘Mathematics for Biologists’
2006 – 2010	Organized Journal Club on Population genetics
2006	Developed and taught Biostat 664/Bioinformatics 800 ‘Statistical population genetics’
2007	Taught Biostat 866 ‘Advanced topics in statistical Genetics’
2009	Taught Biostat 665/Bioinformatics 665/ Human Genetics 665 ‘Statistical population genetics’
2009	Taught Biostat 866 ‘Advanced topics in statistical Genetics’

### ***Individual Lectures***

2005	Various lectures on coalescence theory and evolution.
2006	Instructor for ‘Short course on coalescence theory in association mapping’, Institute Gulbenkian de Cienã, Portugal
2009	Lecture on psychiatric genetics to psychiatry residents
2010	Lectures on coalescence theory and admixture in Biostatistics 666

### ***Invited Intramural Presentations***

- 2005           Bipolar lunch meeting  
                  Statistical genetics journal club  
                  Population genetics journal club
- 2006           Center for Statistical Genetics group seminar  
                  Center for Statistical Genetics group seminar
- 2007           Statistical genetics journal club  
                  Center for Statistical Genetics group seminar  
                  Interdepartmental group seminar
- 2008           Center for Statistical Genetics group seminar  
                  Department of Psychiatry Grand Rounds  
                  Prechter Seminar Series
- 2009           Brown Bag Seminar, Department of Biostatistics  
                  Interdepartmental group seminar

### **Peer-Review Service**

#### ***Manuscript review***

American Journal of Human Genetics	Genetic Epidemiology
American Journal of Medical Genetics	Genome Research
Annals of Applied Statistics	Human Heredity
Annals of Human Genetics	Nature Methods
Archives of General Psychiatry	PLoS Genetics
Bioinformatics	PLoS One
Biometrics	Proceedings of the Royal Society B
Biostatistics	Statistical Applications in Genetics and Molecular Biology
BMC Medical Genetics	Theoretical Population Biology
BMC Genomics	
European Journal of Human Genetics	

#### ***Grant Review***

NSF  
Department of Veteran Affairs  
NIDCR  
Association for the study of infectious disease genetics, Lausanne (Switzerland)  
German Research Foundation (DFG)

### **Committee, Organizational, and Volunteer Service**

#### ***Institutional***

- 2005-2007      Computing committee, Department of Biostatistics
- 2006            Reviewer for the Center for Computational Medicine and Biology pilot grant
- 2006-2010      Genome Science Training Program lecture series organizer
- 2007            Review committee for the Depression Center Innovation Fund

2007-2010 Admissions committee, Department of Biostatistics  
 2008 Review committee for the Center for Genetics in Health and Medicine post doc competition  
 2009-2010 Center for Statistical Genetics group seminar organizer  
 2009-2010 Search committee, Department of Epidemiology  
 2009 Review committee for The Center for Genetics in Health and Medicine Pilot feasibility grants.

***National***

2007 Reviewer for the annual meeting of the American Society of Human Genetics, panel on population genetics.

**Grant support**

***Present and Active***

1 R01 HL90564 (PI: Zöllner) 9/1/07 – 8/31/10 2.4 calendar  
 NIH \$250,000

Computational statistic approaches to gene-environment interaction  
 The goal of this grant is to develop statistical methods to estimate gene-environment interaction both from family data and from samples of unrelated individuals in a genome-wide association (GWA) study.

NIH R01 MH082784 (PI: Ellingrod) 5/1/08 – 4/30/13 1.2 calendar  
 NIMH \$250,000

CLONE: Antipsychotic and folate pharmacogenetics  
 The goal is to advance schizophrenia treatment while accounting for new information about genetic, dietary and lifestyle factors that relate to AAP associated metabolic complications.

R01GM073822-31069 (PI: Zöllner) 3/01/06 – 2/28/10 0.58 academic  
 University of Chicago/NIH - subcontract \$10,300 0.13 summer

Genome wide association mapping in arabidopsis thaliana  
 The goal of this grant was to analyze the generated tiling array data to infer polymorphisms and to then correlate these polymorphisms with phenotypic differences.

R01 MH084698-01 (PI: Abecasis) 9/25/08 – 6/30/11 0.90 academic  
 NIH \$250,000 0.20 summer

Gene mapping of complex traits using resequencing data  
 The goal is to develop statistical methods and software tools that can handle high throughput re-sequencing data including results from shotgun re-sequencing of whole genomes or candidate regions.

***Previous Grants***

No number (PI: Zöllner) 11/01/06 – 11/01/07  
 Rachel Upjohn \$20,000  
 Mapping the genetic heterogeneity of bipolar disorder using clinical traits

This proposal explored the interaction between genetic and environmental determinants of bipolar disorder with the aim to develop a novel and innovative approach to address the problem of genetic heterogeneity.

U01 HL084729-02 (PI: Abecasis) 4/01/06 – 3/31/09  
NIH \$194,118

Integrated parametric and non-parametric mapping for genome-wide association data  
The goal of this grant was to develop and evaluate parametric and non-parametric methods for whole genome association mapping.

R01-MH070775 (PI: McInnis) 11/01/04 - 10/31/09  
NIH \$400,000

Finemapping in 8q24  
The goal of this project was to assess the NIMH sample for evidence of association between bipolar disorder and a locus under the linkage peak on 8q24. The Illumina genotype data is used to infer CNV segregating in this chromosomal region.

### ***Submitted Grants***

(PI: Zöllner) 7/01/10-07/01/15 2.4 calendar  
NIH \$250,000

Advanced strategies for genotype imputation  
This project devises methods to optimize genotype imputation of common and rare variants in population based samples.  
*Reviewed 2/3/10 Impact score 10 Percentile 2.0*

(PI: Liberzon) 7/01/09 – 6/30/14 0.9 academic  
NIH \$1,738,188 0.2 summer

Studies of pathways to prevention: epidemiology of army risk & resiliency  
This project is designed to study and ultimately modify suicide risk factors among those serving in the army.

(PI: Zöllner) 12/01/10-11/30/2014 2.4 calendar  
NIMH \$400,000

Discovery & analysis of rare variants in the 8q24 bipolar disorder linkage region.  
This project aims to sequence 500 individuals in the 8q24 region and to assess the contribution of rare variants to the risk of bipolar disorder. This grant is a competing renewal of MH070775.

(PI: Koopman) 1/01/11 – 12/31/12 1.44 academic  
World Health Org. Polio Research Cmte \$250,892 0.24 summer

Analyzing poliovirus infection transmission and policy options in south Asia  
We will provide polio transmission analyses that inform decisions on strategies to stop transmission in northern India and control imported outbreaks after elimination anywhere.

(PI: Chen) 12/01/10 0.45 academic  
NIH \$176,940 0.10 summer

MicroRNA and the pharmacogenomics of lithium in bipolar disorder

The purpose is to identify Li responsive miRNA species as biomarkers that may be implicated in the genomics basis of Li treatment outcome in BPD.

(PI: Chen)	12/1/10 – 11/30/15	0.90 academic
NIH	\$250,000	0.20 summer

Molecular determinants of altered gene expression in bipolar disorder

The goal is to identify genetic variants responsible for the altered expression of candidate genes in Bipolar Disease..

(PI: Chen)	12/01/10 – 11/30/12	0.90 academic
NIH	\$137,500	0.20 summer

Plasma miRNA's for lithium treatment outcome prediction

The goal is to assess when brain-specific miRNAs induced by lithium treatment and identified as biomarkers in plasma from BPD individuals may serve as the foundation for treatment outcome prediction.