Chia-Ling Kuo

(*as of 11/2011*)

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Research Interests:

Statistical Genetics

- **Genome-wide association analysis:** estimating the effect size distribution accounting for the winner's curse, planning a discovery and/or replication study in terms of a sample size and a number of top-ranking loci to follow up, methods to adjust for multiple testing and biased distribution of extreme statistics due to heterogeneous populations and/or cryptic relatedness
- **Rare variant analysis:** collapsing genetic effects with the adjustment for effect directions
- **Multi-locus association approaches (utilizing functional information)**: genotype-based methods along with a weighting scheme, haplotype-based methods, allele-combination methods, gene-based analysis, pathway analysis, and protein network analysis

Education:

The University of Pittsburgh, Pittsburgh, PA, USA

Ph.D., Biostatistics, 2005 - 2010

- Advisor: Eleanor Feingold
- Dissertation title: Topics in Statistical Methods for Human Gene Mapping
- Committee: Eleanor Feingold, Daniel E. Weeks, Barmada M. Michael, Chien-Cheng G. Tseng

Institute of Statistical Science, Academia Sinica, Taipei, Taiwan

PostMaster, Research Training Program, 2003 - 2004

National Taiwan University, Taipei, Taiwan

M.S., Division of Biostatistics, Department of Epidemiology, 2001 - 2003

- Advisor: John Jen Tai
- Thesis title: A Bayesian Adjustment Approach for Linkage Analysis of Affected Sib-Pair Data with Typing Errors

National Chengchi University, Taipei, Taiwan

B.B.A, Statistics, 1997 - 2001

Research Experiences:

Research Fellow, **National Institute of Environmental Health Sciences**, Biostatistics Branch, RTP, NC, USA

Research Projects (Dr. Dmitri Zaykin, mentor) **2010 - Present**

Novel rank-based approaches for discovery and replication in genome-wide association studies

- Proposed a novel and accurate approximation to the ranking probability that at least j true effects would rank among the top-u SNPs.
- One of applications of this probability is to compute the proportion of false effects among the follow-up SNPs, which is useful to plan a discovery/replication study.

Detecting joint effects of multiple genetic variants via composite haplotype approach

- Proposed an allele combination method for multi-locus association analysis.
- Evaluated it by comparing with few selected genotype-based and haplotype-based methods using data simulated from a variety of genetic models.

Two-stage multi-locus association analysis - collaping SNPs with the adjustment for effect directions

- Proposed a two-stage analysis where it partitions the sample into two proportions and utilizes the effect directions learned from the first stage for the second stage to collapse SNPs to enhance the power.
- Studied the optimal allocation of sample size for the two stages using common and rare variant data with different degrees of linkage disequilibrium.

Planning a replication study after a large-scale study

- Proposed a guideline for planning a replication study in terms of an effective sample size and a number of SNPs to follow up such that the proportion of false effects among the follow-up SNPs and the proportion of significances among the follow-up true effects will be controlled at desired levels.

Research Assistant and Graduate Studies, **University of Pittsburgh**, Biostatistics, Pittsburgh PA , USA

Genetics of Age-Related Maculopathy (Dr. Daniel Weeks, mentor) **2009 - 2010**

- Responsible for managing a database and using the genetic and environmental data to identify susceptibility loci (database management, data cleaning, association analysis, etc.)
- Collaborated with the laboratory of Dr. Yvette Conley at the University of Pittsburgh and the laboratory of Dr. Michael Gorin at the University of California, Los Angles

Human QTL Mapping with Selected Sampling (Dr. Eleanor Feingold, mentor) **2005 - 2010**

- Compared a number of denominators for the score statistic including novel ones we proposed using sibship data or extended family data with various trait distributions, ascertainment schemes, and distribution of pedigree types
- Developed the QTL-ALL (Quantitative Trait Locus - Association and Linkage Library) software

What's the best statistic for a simple test of genetic association in a case-control study? **2006 - 2008**

- Compared a bunch of genetic association tests and logistic regression models for a SNP and a binary exposure using case-control data in the scopes of single-locus analysis, scans with covariates, and genome-wide analysis.

Research Assistant, **Institute of Statistical Science Academia Sinica**, Taipei, Taiwan

Research projects (Dr. Hsiuying Wang, mentor) **2004 - 2005**

- Assisted in a study on statistical inference mainly through statistical simulation
- Collaborated with Dr. Hsiuying Wang in a research project on modeling genotyping errors in linkage and association analysis

Research Student, **Institute of Statistical Science Academia Sinica**, Taipei, Taiwan

Research training program (Dr. Yi-Hau Chen, mentor) **2003 - 2004**

- Competitively admitted because of outstanding performance in public examinations on linear algebra and calculus, probability & statistics, and English
- Trained with Dr. Yi-Hau Chen and used the textbook "Mathematical and Statistical Methods for Genetic Analysis by Kenneth Lange"
- Courses taken: advanced probability, data analysis, weekly seminars, and other academic activities

Graduate Student, **National Taiwan University**, Taipei, Taiwan

A Bayesian Adjustment Approach for Linkage Analysis of Affected Sib-Pair Data with Typing Errors (Dr. John Jen Tai, mentor) **2001 - 2003**

- Proposed to adjust the mean test with posterior weights
- Modeled the IBD gene frequencies with Dirichlet distribution
- Used the posterior distribution to constructed a weighted mean test statistic

Undergraduate Research Assistant, **National Taiwan University**, Taipei, Taiwan

Research projects (Dr. Chwan-Chuen King, mentor) **2000 - 2001**

- Involved in serval key research projects including: association of climatic factors with epidemics of dengue, immuno-epidemiological studies of dengue fever and dengue hemorrhagic fever, evaluation of Japanese encephalitis (JE) vaccine in neutralizing currently circulating JE viruses in Taiwan and the established syndromic surveillance system for infection disease
- Responsible for solving biostatistical problems and questions

Publications:

Peer-reviewed Manuscripts:

- Bhattacharjee S, **Kuo CL**, Mukhopadhyay N, Brock GN, Weeks DE, Feingold E (2008). Robust Score Statistics for QTL linkage analysis. **Am J Hum Genet** *82*: 567-582.
- **Kuo CL**, Feingold E (2009). What's the best statistic for a simple test of genetic association in a case-control study? **Genetic Epidemiol** *3*4: 246-253.
- McKay GJ, Silvestri G, Chakravarthy U, Dasari S, Fritsche LG, Weber BH, Keilhauer CN, Klein ML, Francis PJ, Klaver CC, Vingerling JR, Ho L, de Jong N, Dean M, Sawitzke J, Baird PN, Guymer RH, Stambolian D, Orlin A, Seddon JM, Peter I, Wright AF, Hayward C, Lotery AJ, Ennis S, Gorin MB, Weeks DE, **Kuo CL**, Hingorani AD, Sofat R, Cipriani V, Swaroop A, Othman M, Kanda A, Chen W, GR Abecasis GR, JR Yates JR, AR Webster AR, AT Moore AT, JH Seland JH, Rahu M, Soubrane G, Tomazzoli L, Topouzis F, Vioque J, Fletcher AE, Patterson CC (2011). Variations with age in Apolipoprotein E frequency in a pooled analysis of a large group of older people. **Am J Epidemiol** *173*: 1357-1364.
- **Kuo CL** and Zaykin D (2011) Novel rank-based approaches for discovery and replication in genome-wide association studies. **Genetics** *189*: 329-340.
- McKay GJ, Patterson CC, Chakravarthy U, Dasari S, Klaver CC, Vingerling JR, Ho L, de Jong PT, Fletcher AE, Young IS, Seland JH, Rahu M, Soubrane G, Tomazzoli L, Topouzis F, Vioque J, Hingorani AD, Sofat R, Dean M, Sawitzke J, Seddon JM, Peter I, Webster AR, Moore AT, Yates JR, Cipriani V, Fritsche LG, Weber BH, Keilhauer CN, Lotery AJ, Ennis S, Klein ML, Francis PJ, Stambolian D, Orlin A, Gorin MB, Weeks DE, **Kuo CL**, Swaroop A, Othman M, Kanda A, Chen W, Abecasis GR, Wright AF, Hayward C, Baird PN, Guymer RH, Attia J, Thakkinstian A, Silvestri G (2011). Evidence of association of APOE with age-related macular degeneration - a pooled analysis of 15 studies. **Hum Mutat** *32*: 1407-1416.

Papers in Progress:

- **Kuo CL**, Bhattacharjee S, Mukhopadhyay N, Weeks DE, and Feingold E. Robust score statistics for QTL linkage analysis using extended pedigrees.
- **Kuo CL**, and Zaykin D. Detecting joint effects of multiple genetic variants via composite haplotype approach.
- **Kuo CL**, and Zaykin D. Planning a replication study after a large-scale study.

Conference publications:

- Bhattacharjee S, **Kuo CL**, Mukhopadhyay N, Weeks DE, and Feingold E. A comparison of robust methods for QTL mapping in nuclear families, in the *56-th* annual meeting of American Society of Human Genetics. New Orleans, Louisiana. October, 2006.
- Mukhopadhyay N, Bhattacharjee S, **Kuo CL**, Weeks DE, and Feingold E. QTL-ALL: software for QTL linkage analysis using score statistics and other new approaches, in the *56-th* annual meeting of American Society of Human Genetics. New Orleans, Louisiana. October, 2006.
- Bhattacharjee S, **Kuo CL**, Mukhopadhyay N, Brock GN, Weeks DE, and Feingold E. Robust methods for QTL linkage analysis in nuclear families, in the *57-th* annual meeting of American Society of Human Genetics. San Diego, California. October, 2007.
- **Kuo, CL**, and Feingold E. What's the best statistic for a simple test of genetic association in a case-control study?, in the *57-th* Annual Meeting of American Society of Human Genetics. San Diego, California. October, 2007.

- **Kuo, CL**, and Feingold E. What's the best statistic for a simple test of genetic association in a case-control study?, in the Joint Statistical Meetings of American Statistical Association. Denver, Colorado. August, 2008.
- **Kuo, CL**, and Feingold E. What's the best statistic for a simple test of genetic association in a case-control study?, in the *18-th* Annual Meeting of International Genetic Epidemiology Society. Kahuku, Hawaii. October, 2009.
- **Kuo CL**, Bhattacharjee S, Mukhopadhyay N, Weeks DE, and Feingold E. Robust score statistics for QTL Linkage Analysis using extended pedigrees, in the *59-th* Annual Meeting of American Society of Human Genetics. Honolulu, Hawaii. October, 2009.
- Huang EI, and **Kuo CL**. Fourier patterns represent tone-burst and click response latencies in auditory nerve fibers, in the Epistemology of Modeling and Simulation Conference, Pittsburgh, Pennsylvania. April, 2011.
- **Kuo CL**, and Zaykin DV. Detecting joint effects of multiple genetic variants via composite haplotype approach, in the Joint Statistical Meetings of American Statistical Association. Miami, Florida. August, 2011.
- Zaykin DV, and **Kuo CL**. Novel rank-based approaches for discovery and replication in genome-wide association studies, in the Joint Statistical Meetings of American Statistical Association. Miami, Florida. August, 2011.
- Zaykin DV, and **Kuo CL**. Novel rank-based approaches for discovery and replication in genome-wide association studies, in the *12-th* International Congress of Human Genetics, Montreal, Quebec. October, 2011.
- **Kuo CL**, and Zaykin DV. Two-stage multi-locus association analysis - collapsing SNPs with the adjustment for effect directions, in the *12-th* International Congress of Human Genetics, Montreal, Quebec. October, 2011.

Presentations:

Invited Seminars:

- Novel rank-based approaches for discovery and replication in genome-wide association studies, National Institute of Environmental Health Science, Research Triangle Park, North Carolina. October 2011.

Conference Posters:

- What's the best statistic for a simple test of genetic association in a case-control study?, at the *57-th* Annual Meeting of American Society of Human Genetics. San Diego, California. October, 2007.
- What's the best statistic for a simple test of genetic association in a case-control study?, at the *18-th* Annual Meeting of International Genetic Epidemiology Society. Kahuku, Hawaii. October, 2009.
- Robust score statistics for QTL Linkage Analysis using extended pedigrees, at the *59-th* Annual Meeting of American Society of Human Genetics. Honolulu, Hawaii. October, 2009.
- Two-stage multi-locus association analysis - collapsing SNPs with the adjustment for effect directions, presented at the *12-th* International Congress of Human Genetics, Montreal, Quebec. October, 2011.

Conference Talks:

- What's the best statistic for a simple test of genetic association in a case-control study?, at the Joint Statistical Meetings of American Statistical Association. Denver, Colorado. August, 2008.
- Detecting joint effects of multiple genetic variants via composite haplotype approach, presented at the Joint Statistical Meetings of American Statistical Association. Miami, Florida. August, 2011.

Teaching Experiences:

Division of Biostatistics, Department of Epidemiology, National Taiwan University, Taipei, Taiwan

Biomedical Statistics of the Medical School, Teaching Assistant **2001 to 2003**

- Graded homeworks and exams
- Coordinated with other TAs
- Tutored graduate students with their homework

Awards and Honors:

- Paper of the month, **Kuo CL, Zaykin D (2011) in Genetics 189(1): 329-340**, chosen by the NIEHS Division of Intramural Research (DIR) leadership (2011)
- **Student of the Year award**, American Statistical Association Pittsburgh chapter (2010)
- **First Place in the National-wide College Entrance Examination in the department of Statistics**, National Chengchi University, Taipei, Taiwan (1997)

Technical Skills:

- **Programming:** R, SPLUS, SAS (certified base programmer for SAS 9), C, Python, Mathematica, MySQL
- **Applications:** LaTeX, BibTeX, Microsoft Office, and other common productivity packages for Windows and Linux platforms
- **Operating Systems:** Microsoft Windows XP, MacOS and Linux/Unix

Research-related Activities:

- Attended a one-week course entitled **Complex Trait Analysis** organized by Jackson Laboratory at Bar Harbor, Maine, October 2007
- Attended a one-week course entitled **Advanced Gene Mapping** organized by Rockefeller University at New York, New York, December 2008

Services:

Manuscript Review:

- Refereed articles for journals including Biometrics, Biostatistics, and Annals of Human Genetics
- Intramural Review for the National Institute of Environmental Health Sciences

Book Review:

- Siegmund, D, Yakir, B (2010) The Statistics of Gene Mapping

Editorial Boards:

- 2011-present, Editorial Board, Frontiers in Applied Genetic Epidemiology

Professional Organizations:

- American Society of Human Genetics (2007 - present)
- American Statistical Association (2008 - present)
- International Genetic Epidemiology Society (2009 - 2010)

Personal:

- **Gender:** Female
- **Citizenship:** Taiwan
- **Languages:** English and Chinese (Mandarin)

References:

Dr. Dmitri Zaykin
Principal Investigator, Biostatistics Branch,
National Institute of Environmental Health Sciences
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Dr. Eleanor Feingold
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Dr. Daniel E. Weeks
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Office: 412-624-5388
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