

Statfax

Spring Meeting Workshop

The Spring 2008 will be held on Thursday, March 13, 2008. There will be three speaker sessions covering a variety of topics:

A new method to identify significant endpoints in a closed test setting.

When testing several hypotheses simultaneously, the challenge is to combine them into a multiple test procedure that controls the familywise error rate, or overall α . One useful approach is the closure method. We develop a powerful statistical test for use with the closure method for testing co-primary endpoints in clinical trials, when there is a common effect direction and the test statistics are normally distributed. We show that the simple sum test is maximin, then alter its rejection region to make it consonant, i.e., to guarantee that rejection of the intersection hypothesis implies that at least one endpoint is significant. This new test has greater power and retains the maximin property. Our application to PROactive, a CV-outcome trial of patients with Type 2 DM and CV disease history, shows how efficacy for one key endpoint could have been established. Taking the primary and secondary endpoints as co-primary, in a closed test design, both the simple sum test and the consonant sum test yield p-values below the allocated α .

Challenges in statistical modeling of chromatin sequence for eukaryotic species

As evidence aggregates showing that DNA sequence itself is the determinant factor in nucleosome positioning in Eukaryotic cells, statistical modeling of chromatin sequence remains exceedingly challenging. The challenges arise as a consequence of the fact that the signals intrinsic in nucleosome sequences are very weak; in addition knowledge on the linker DNAs, which are interwoven with nucleosome motifs in chromatin fiber, is very limited. In particular the linker length, which determines the orientation of adjacent nucleosomes, is of fundamental importance in understanding chromatin structure. We investigate the linker length distribution of two Eukaryotic species including yeast and human using two novel methods: a Fourier analysis of dinucleotide frequency in the extended region of nucleosome core particles and a duration Hidden Markov Model (DHMM) for dinucleosome sequences. Both methods conclude that the linker length distribution is not uniform but periodic. The DHMM method further shows that the linker length prefers a form $10n + d_0$, where $d_0 = 5$ bp for yeast as opposed to 10 bp for human overwhelmingly.

Important Statistical considerations in biomarker discovery and clinical evaluation

The quality of statistical thinking and methods used is a major determinant in the

successful discovery and evaluation of biomarkers. Data normalization and transformation methods can greatly impact the analysis. False discovery rates (q-values) and miss rates are critical for setting meaningful thresholds for identification.

While it is important to analyze each marker individually (e.g., ANOVA), it is also important to keep in mind that *a marker useless on its own may be great in a composite*. The use of multivariate modeling methods that account for the interactions, similarity and diversity of the markers is essential for the identification of composite biomarkers. Examples of such methods include generalized additive models, shrunken centroids, random forests, kNN clustering, etc. The predictive utility of these composite biomarkers should be assessed carefully via appropriate internal cross-validation methods, and further tested in independent cohorts (external validation) to expand and qualify their use in early drug development. In addition, the statistical evaluation of validation data from biomarker analytical platforms can have a major impact on the utility of such platforms. This short presentation will provide some background on biomarker research and an understanding of all these statistical considerations with illustrations and graphs.

Speaker Bio's

Dr. Viswanath Devanarayan received his Ph.D. in Statistics from NC State, 1996. He has 12 years of experience in the pharmaceutical industry, spanning Lilly, Merck and Abbott. His primary areas of focus included drug discovery applications, assay methodologies, clinical pharmacology, experimental medicine, and biomarker discovery and evaluations in both pre-clinical and clinical applications. In all of these topics, he has given numerous invited

presentations at various international meetings. As part of some committees within PhRMA, AAPS, AACR, SBS, etc., he has coauthored with relevant subject-matter experts from other companies, FDA, academia and NIH, in important position papers related to immunogenicity, high throughput screening, biomarker method validation and clinical biomarker qualification.

Dr. Carlos Vallarino has been working in the pharmaceutical industry for the past 7 years. Following 3 years in Phase II/III clinical trials at Eli Lilly and Pharmacia, he joined Takeda's Outcomes Research group in 2003, where the emphasis is on the analysis of Phase IV outcomes from claims databases. He recently transferred to the Epidemiology group, where he has expanded his responsibilities to include the statistical analysis of safety data, particularly early signal detection. Dr. Vallarino holds a Bachelor's degree in Mathematics, Economics and Statistics from the State University of New York at Buffalo, Master's and Ph.D. degrees in Statistics from the University of California at Berkeley.

Dr Ji-Ping Wang earned his Ph.D. degree in statistics from Penn State University in 2003. He has been an assistant professor in statistics at Northwestern University since then. His current research focuses on two areas: (1) mixture model, computing algorithms and applications; (2) bioinformatics and computational biology. His research topics include penalized NPMLE and algorithm for species richness estimation, Expressed Sequence Tag (EST) data analysis, nucleosome sequence alignment and prediction and human brain mapping. He has been publishing in journals including JASA, Nature, Bioinformatics, BMC Bioinformatics, NAR, PLoS

Computational Biology etc. His research has been supported by NSF/NIGMS and NIH.

President's Report

Greetings to everyone and Happy New Year! We are very fortunate to have a great program of speakers lined for our Spring meeting on March 13. Dr. Carlos Vallarino will be presenting his work in identifying endpoints in clinical trials, Dr. Jiping Wang will present a paper on statistical modeling, and Dr. Devanarayan will be presenting his work in the area of Biomarkers. The summer workshop date has also been finalized – mark your calendars for Thursday, June 5. Dr. Garrett Fitzmaurice will present his workshop in “Applied Longitudinal Analysis.”

Many thanks to everyone who has worked to support the Northeastern Illinois Chapter of the American Statistical Association (NIC-ASA) over the years. I think we are especially fortunate in our very diligent and hard-working past president, Melvin Munsaka, who has continued to be at the forefront in service to our Chapter. I am very grateful for his assistance as I find my way in my new role for this year as your current Chapter president. I also would like to thank our 2007 program committee: Melvin Munsaka, Joan Chmiel, Bala Hosmane, Jeff Isaacson, and our new program chair for 2008: Xuejun Peng, who has been very busy lately finalizing last-minute arrangements for our speakers on March 13.

Our executive committee this year includes a number of folks who have been serving our chapter for quite a few years now. In addition to Xuejun Peng, who has accepted the position of President Elect/Program Chair for this year, our continuing executive committee members include Melvin Munsaka (past president), Jeff Isaacson (chapter representative), Sandra Sinisi (secretary),

Zhen Zhao (treasurer), Carolyn Setze (arrangements), Carl Slenk (newsletter), Richard Rode (publicity), Michelle Olds (webmaster), Sam Hedayat (Awards and Recognition), Carole Bennett and Paul Coe (Community Activities), and Colleen Hall (listserv). Many thanks to all for your service to our chapter.

We are always in need of additional volunteers to support chapter activities. There is presently an opening for Newsletter Associate Editor. If you are interested in that position or if you would like to take an active role in another capacity promoting our chapter please contact me or any member of the Executive Committee.

I wish everyone a prosperous and healthy 2008. I look forward to seeing many of you at our chapter meetings.

~ Anita Ross

Employment Opportunities

Statistician/Analytic Programmer. Exciting opportunity to work with growing research group investigating ways to help people lead healthier lives. Responsibilities include SAS programming; models used include linear and logistic regression, survival analysis, longitudinal analyses, analyses of missing data. Research designs include longitudinal epidemiological studies as well as clinical trials. Master's degree in statistics or biostatistics required. Experience with SAS required; experience with S-Plus or SPSS a plus. New graduates and more experienced persons both welcome to apply; salary commensurate with prior experience. The strong candidate will be able to understand a research problem, implement the appropriate statistical methods in consultation with a senior statistician, review diagnostics of model appropriateness, and communicate the results both orally and in writing. Opportunity

for direct collaboration with investigators, based on knowledge and experience. Cover letter and c.v. to Dr. Julia Bienias, Director, Section of Biostatistics and Epidemiology, Dept. of Preventive Medicine, Rush University Medical Center, 1700 W. Van Buren, Suite 470, Chicago, IL 60612. jbienias@rush.edu. EOE.

Chapter Website

Don't forget to visit our Chapter web page at <http://www.amstat.org/chapters/NortheasternIllinois>. The website has lots of information about our Chapter, including events, program information, and contact information for Chapter officers and committee members. You can also peruse PDF versions of current and past Chapter newsletters. Finally, if the speaker provides them, slides/notes from previous presentations are available to view or download.

Calendar

Chicago Chapter ASA Workshop Announcement

Short Course on Applied Survival Analysis

Presenter: Susanne May, University of California, San Diego

Date: Friday, 14 March 2008, 8:30-5:00

Venue: Gleacher Center

450 North Cityfront Plaza Drive
Chicago, IL 60611-4316
312-464-8787

Course Outline

The course does not assume prior knowledge of survival analysis techniques, but familiarity with either linear or logistic regression is assumed. Mathematical details are kept to a minimum. Approaches will be illustrated with examples from health-related studies.

- Introduction to survival analysis
 - Survival analysis data
 - Descriptive methods
 - Comparison of survival functions
- Regression modeling of survival data
 - Fitting the Cox proportional hazards model
 - Interpretation of the fitted model
 - Model building strategies
 - Assessing model adequacy
- Extensions of the proportional hazards model
 - Stratified proportional hazards model
 - Time-varying covariates
- Other topics
 - Frailty models
 - Sample size and power

Early Registration Fees

Student \$95

Member \$395

Non-member \$495

After March 1, add \$50 to the early registration fees.

The fee includes extensive materials and a copy of the book "Applied Survival Analysis: Regression Modeling of Time to Event Data, 2nd ed.," breakfast items, lunch, and refreshments for AM and PM breaks. Space is limited. To ensure yourself a place, please register early.

For More Information Contact: Tony

Babinec, VP Workshops

(tbabinec@sbcglobal.net) and or visit the

chapter website: <http://www.chicagoasa.org/>.

~Melvin Munsaka

May 19-21 – Thirty-First Annual Midwest Biopharmaceutical Statistics Workshop (MBSW)

The workshop will be held on the campus of Ball State University in Muncie, Indiana. Some of this year's workshop sessions will be held at the Horizon Conference Center downtown Muncie. It is co-sponsored by Ball State University and the Biopharmaceutical Section of ASA. A ½-day short course will be taught by Michael Proschan on Statistical Monitoring of Clinical Trials: A Unified Approach. The plenary speakers will include Jerome Friedman who will speak on Generalized Boosting Algorithms for Regularized Regression and Classification, and Rod Little who will discuss Missing Data in Clinical Trials. Peter Lachenbruch will deliver the banquet speech and will discuss Communicating Statistics: Speaking Out and Reaching Out. Invited talks will be presented in four parallel tracks: the **Clinical** track will focus on current issues in clinical trials, including sessions on Adaptive Designs in Dose-Ranging Studies, Meta-Analysis of Clinical Trial Data, and Experimental Medicine and Biomarker Use in Clinical Trials; the **Discovery/Preclinical** track will focus on statistical issues in the design and analysis of -omics experiments and will include sessions on Toxicogenomics, Proteomics: Statistical Methods for an Emerging Technology, and Statistical Issues and Analyses of Metabolomics Data; the **Non-Clinical** track will focus on statistical contributions to CMC development, manufacturing, and quality control with sessions on Quality by Design, Critical Process Parameters, Critical Quality Attributes and Control Strategies, and Stability Analysis Methods; the **Post Marketing** track will focus on assessing medicines post-launch and will include sessions on Pharmacovigilance, Defining Benefit/Risk, and Statistical Issues in Observational Studies. There will also be a

contributed Poster Session. Poster abstracts must be submitted by April 21, 2008. Students may submit posters for the Charlie Sampson Award. **More Information:** A preliminary program, registration form, and other information are located at www.mbswonline.com. Or, contact the Publicity Chair Melvin Munsaka, Takeda Global Research & Development, Inc., email mmunsaka@tgrd.com, phone (224)-554-5912

~Melvin Munsaka

Publication Info

Statfax is published three times a year (Spring, Summer, and Fall), by the Northeastern Illinois Chapter of the American Statistical Association.

Statfax welcomes letters and material for articles from its readers. Address correspondence to: The Editor, Statfax, c/o Carl Slenk, Abbott Molecular, 1300 E. Touhy Ave., Des Plaines IL 60018

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The Chapter's purpose, as stated in its Constitution, is "to foster statistics and its applications and promote the interests of the statistical profession...". Accordingly, diverse views are presented. They do not necessarily reflect the opinions of the officers or the policies of the Chapter