

FRONTIERS OF EVOLUTIONARY BIOLOGY

Nothing in biology makes sense except in the light of evolution.
- Dobzhansky

ONE DAY WORKSHOP
FRIDAY, OCTOBER 10, 2008
HUB AUDITORIUM

Keynote Speakers

ELIZABETH THOMPSON

P.R. Krishnaiah Visiting Scholar: 2008

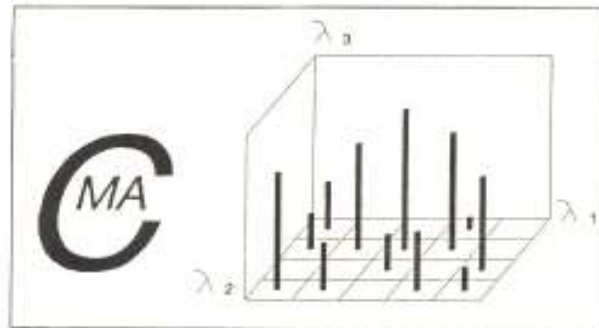
*Inference of genome sharing among related individuals:
Integrating modern SNP data on pedigrees and populations*

and

ALAN WALKER

C.G. Khatri Visiting Scholar: 2008

Humans in an evolutionary context



The Center for Multivariate Analysis
Department of Statistics

PENNSSTATE



Frontiers of Evolutionary Biology

One day Workshop: October 10, 2008

HUB Auditorium

- 9:00-9:05 Welcome by **Daniel J. Larson**
Dean, Eberly College of Science, PSU
- 9:05-9:15 **Masatoshi Nei** (Chairman)
Introduction of Topic and Speakers
- 9:15-10:05 **Elizabeth Thompson**
Inference of genome sharing among related individuals:
Integrating modern SNP data on pedigrees and
populations.
- 10:05-10:15 Discussion
- 10:15-10:30 Tea break
- 10:30-11:00 **Kateryna Makova**, PSU
Studying mutations in the age of statistical genomics.
- 11:00-11:30 **Yu Zhang**, PSU
Reconstructing evolution history for complex gene
clusters in multiple primates
- 11:45-1:15 *"Flock of Dodos: The Evolution/Intelligent-design
circus"* a movie by Randy Olson
- 1:15-2:15 Lunch break
- 2:15-2:25 **Peter Hudson** (Chairman)
Introduction of Topic and Speakers
- 2:25-3:15 **Alan Walker**
Humans in an evolutionary context
- 3:15-3:25 Discussion
- 3:25-3:55 **Beth Shapiro**, PSU
Inferring the demographic history of measurably
evolving populations using ancient DNA
- 3:55-4:25 **Adam Siepel**, Cornell University
Phylogenomics of mammals: Novel genes and positive
selection
- 4:25-4:45 Discussion on all topics

Parachuri R. Krishnaiah Visiting Scholar
Professor Elizabeth Thompson
University of Washington



Elizabeth Thompson is Professor of Statistics and Adjunct Professor of Biostatistics and of Genome Sciences at the University of Washington in Seattle. She received Ph.D. in Statistics (1974), and Sc.D. degree from the University of Cambridge.

Thompson has published four research monographs and over 115 refereed papers in the scientific statistical literature. Her research focuses on the development of models and of likelihood-based methods for inference from genetic and genomic data, particularly data observed on related individuals whether in structured populations or as members of large and complex pedigree structures.

She is an elected a member of the International Statistical Institute (1981), and a Fellow of the American Academy of Arts and Sciences (1998). She received the inaugural Jerome Sacks Award for Outstanding Cross-Disciplinary Research from the National Institute for Statistical Sciences, and the Weldon Prize for contributions to Biometric Science from the University of Oxford (2001). She has held a Guggenheim Fellowship (2002-2003), and a Rothschild Visiting Professorship at the University of Cambridge (2006). In 2008, she was elected a member of the U.S. National Academy of Sciences.

Twenty-three students have obtained Ph.D.'s working under Thompson's supervision. Of these, sixteen now hold university faculty positions, and four hold research positions in industry or the nonprofit sector.

**C.G. Khatri Visiting Scholar
Professor Alan Walker
Penn State University**



Alan Walker, Fellow of Royal Society, U.K., Member of American Academy of Arts and Sciences, and Foreign Member of National Academy of Sciences, USA, is Evan Pugh Professor of Anthropology and Biology at Pennsylvania State University. He is a world renowned paleoanthropologist who works on primate and human evolution. He is the author of over 180 scientific papers and author or editor of several books on evolution, and is listed by ISI as highly cited author (2002). He is the recipient of the International Fyssen Foundation (Paris) Prize, Penn State University Faculty Scholar's Medal, Hon.D.Sc. from University of Chicago, Distinguished Membership of National Society of Collegiate Scholars. Professor Walker's main interest is in extracting ancient behaviors from the fossil and taphonomic record. Teeth record information about an individual's life history and semicircular canals are tuned to a species' rapidity of locomotion. He is now developing nondestructive methods for examining tooth enamel and measuring fossil labyrinths so that rare hominoid and hominid specimens can be used.

ABSTRACTS OF TALKS

Elizabeth Thompson

Inference of genome sharing among related individuals: Integrating modern SNP data on pedigrees and populations.

Abstract: Similarities among individuals for quantitative traits determined in whole or in part by their DNA arise from the coancestry of these individuals. Related individuals share segments of their genome, in the sense that these segments derive from a single DNA segment in a common ancestor. Such segments are said to be identical-by-descent or ibd and have high probability of being of the same biochemical type. While a known pedigree relationship gives a probability distribution on the marginal probability of ibd and on lengths of ibd segments, modern genomic data permits much more precise inference of shared genome. A new model for ibd sharing among multiple genomes will be presented, and its use in ibd inference from genomic data demonstrated. Then, given such inferred ibd, known pedigree relationships and unknown population relationships among individuals can be combined in the analysis of phenotypic data on genetic traits, providing greater sensitivity and specificity in localizing DNA that affects the trait of interest.

Kateryna Makova

Studying mutations in the age of statistical genomics

Abstract: Evolution starts with and is impossible without mutations. Yet, mutations are rather infrequent and therefore are difficult to study. However, with completely sequenced genomes accumulating at a growing pace, bioinformatic and statistical analyses of mutations are now feasible. It is known that mutation rates fluctuate greatly from locus to locus in mammalian genomes, and that the rates of some mutation types co-vary regionally. The causes of this variation and co-variation remain largely unexplored, and deciphering them computationally is expected to unravel the intricacies of mutagenesis. Compared with wet-lab experiments, computational analyses enable us to study mutations in their native genomic environment and on a whole-genome scale. In this presentation I will focus on our recent studies of regional variation of indel, microsatellite, and substitution rates, which employ regression methods. Additionally, I will present some novel results on the motif context of indel mutations (investigated with the use of wavelet transformation techniques) as well as on regional co-variation among rates of mutations of different types (studied with Canonical Correlations Analysis).

Yu Zhang
Reconstructing evolution history for complex gene clusters in multiple primates

Abstract: Complex gene clusters evolved from single progenitors via repeated segmental duplications are abundant in primate genomes. Such clusters serve as a hotbed of functional innovation that makes them extremely interesting. An initial analysis of human complex gene clusters has revealed distinct tempos of large-scale evolutionary events in several disease-related gene clusters, where some clusters evolved anciently before the advent of human, and others evolved exclusively in the human lineage. Given the very complex nature of this problem and the data quality, we introduce an importance sampling algorithm in an attempt to simultaneously reconstructing several plausible evolutionary histories of multiple primate gene clusters. One of the main challenges in multi-species evolution reconstruction is the coalescence of species. We demonstrate that using ortholog information can help resolving this issue adequately.

Alan Walker
Humans in an evolutionary context

Abstract: As people grow up they develop the illusion that they are an entirely individual being. But we are really complete ecosystems with our own bacterial flora and fauna and parasites and much of our DNA, even, made of viral sequences. And we exist in bigger ecosystems that change all the time just as we do. Although we imagine ourselves to be perfectly integrated functional entities, we are made of parts that have been added together and adjusted through evolutionary compromise over enormous amounts of time. Some of our parts have ancient origins and others have been added much later. The fossil record and comparative anatomy and genomics allows us to tell which parts were added when, and in some cases why.

Beth Shapiro
Inferring the demographic history of measurably evolving populations using ancient DNA

Abstract: The recent development of ancient DNA (aDNA) techniques to extract genetic material from fossil remains as old as 100,000 years has revolutionized population genetics. Rather than analyzing single "snapshots" of diversity, this technique makes it possible to go back in time and directly measure changes in genetic diversity over considerable time periods. The simultaneous development of statistical methods driven by Coalescent theory and implemented within a sophisticated Bayesian inference framework has allowed real-time reconstruction of demographic changes in populations and communities. Our inference framework allows explicit tests of how populations are affected by environmental events such as ice ages or other dramatic changes in climate, and by community-level changes such as competition or the

introduction of human predators. Using data from six different species that were once widely distributed across the Northern hemisphere: mammoth, lions, bison, bears, horses and muskoxen, I will attempt to reconstruct the Late Pleistocene Beringian faunal community, and investigate the relative roles of climate change and human hunting in the demise of the Pleistocene megafauna. Together, these analyses reveal a tumultuous evolutionary history for all six taxa over the last 100,000 years, including multiple occurrences of population turnover, bottlenecks and local extinctions and replacements, all which argue strongly (and often disconcertingly) that inference based on modern data alone is likely to be misleading. Finally, I will discuss some of the current challenges to using measurably evolving data, and in particular aDNA, in demographic inference.

Adam Siepel

Phylogenomics of mammals: Novel genes and positive selection

Abstract: I will describe two recent comparative genomics projects in mammals. The first is a large-scale effort, carried out as part of the Mammalian Gene Collection (MGC) project, to identify human genes not yet in the gene catalogs. Our approach was to produce gene predictions by algorithms that rely on comparative sequence data but do not require direct cDNA evidence, then to test predicted novel genes by RT-PCR. This work led to the identification of more than 2000 novel exons corresponding to an estimated ~500 genes, including >160 that were completely absent from the gene catalogs. The second project is a comprehensive analysis of positively selected genes (PSGs) in mammals based on the six high-coverage eutherian mammalian genome assemblies now available. Compared with previous genome-wide scans for PSGs, the increased phylogenetic depth of this data set results in substantially improved statistical power, and permits several new lineage- and clade-specific tests to be applied. Several hundred apparent PSGs were identified, and a detailed analysis was performed of their selection histories (evolutionary patterns of selection and nonselection), the functional categories and pathways to which they belong, and their expression patterns. Together, these projects illustrate the power of comparative genomics in characterizing evolutionary dynamics, selection pressures, and genomic function.

CENTER FOR MULTIVARIATE ANALYSIS

The Center for Multivariate Analysis is an interdisciplinary research unit within Penn State's Department of Statistics. Established in 1982 at the initiative of the Air Force Office of Scientific Research, it is the first research center in the world with a primary focus on multivariate analysis. C.R. Rao, Emeritus Professor of statistics and Holder of the Eberly Family Chair, is the director of the center.

One function of the Center for Multivariate Analysis is to create opportunities for scholars from all over the world to visit and conduct research. Statistical researchers from countries such as China, India, Japan, from Europe and the United Kingdom have visited the center.



P.R. Krishnaiah
(7/15/32-8/1/87)



C.G. Khatri
(8/8/31-3/31/89)

P.R. Krishnaiah was the founder-director of the Center for Multivariate Analysis. He received numerous honors and international recognition for his outstanding contributions to the theory and applications of Statistics.

C.G. Khatri was a frequent visitor to the Center for Multivariate Analysis. He has authored or co-authored several books and about two hundred research publications in prestigious journals.

In order to perpetuate the memory of P.R. Krishnaiah and C.G. Khatri, a Visiting Scholars Program has been started at Penn State. Under this program, outstanding scholars are invited to visit the CMA to give lectures and/or participate in research work. Donors are kindly requested to send their contributions by check drawn in favor of "Penn State Krishnaiah Memorial Fund" and/or "Penn State Khatri Memorial Fund" to Development Office, Penn State Eberly College of Science, 430 Thomas Building, University Park, PA 16802-2111. Penn State will be the custodian of these funds and the donations are tax deductible.

This publication is available in alternative media on request.

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