Biostatistics & Computational Biology

2010 Annual Newsletter

Dear Colleagues,

As I write this introduction to the third annual newsletter for the Department of Biostatistics and Computational Biology in February 2011, we are looking forward to our upcoming move in April to the top floor of the new Clinical and Translational Science Building here at Rochester. We will all now be very busy sorting and packing in preparation for the move.

This has been another successful year academically, as well as socially, as you will see from the following pages. We expect another good year in 2011.

We are always eager to hear news, formal or informal, from our graduates and friends. Please send any items to susan_divincenzo@urmc.rochester.edu or newsletter@bst.rochester.edu

David Oakes

The Future Home of Biostatistics and Computational Biology

NIH-NIAID supports the development of mathematical models and statistical methods as important tools to fight against infectious diseases

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), recently awarded an $11.9 million contract to the University of Rochester (UR) Medical Center to continue the work of the Center for Biodefense Immune Modeling (CBIM) for another five years. The co-directors of the UR-CBIM are **Dr. Hulin Wu,** Professor of Biostatistics, Department of Biostatistics and Computational Biology, and **Dr. Martin Zand**, Professor in the Department of Medicine at the UR Medical Center. The Center provides a good example for successful collaborations between quantitative scientists and experimental investigators.

This successfully awarded renewed proposal builds on the work of the UR-CBIM, which was established five years ago, with the original total award of $10 million. During the past five years, the UR-CBIM, composed of a multi-disciplinary team of statisticians, mathematical and engineering modelers, computer scientists, software developers, bioinformaticians, and biomedical investigators, sought to develop novel mathematical models, statistical methods, and bioinformatics tools to decipher the host immune responses to influenza infection and other infectious agents. Extensive experimental data from mice were collected to support the development and validation of the proposed models, statistical methods, and bioinformatics tools. This project resulted in 60 manuscripts (50 published/accepted and 10 submitted or under revision) over the past five years: 10 in biomathematical modeling journals, 27 in statistical or biostatistical journals, 5 in bioinformatics/biocomputing journals, and 18 in biomedical science journals. Many of these papers were published in top statistical/biostatistical journals such as *JASA*, *Annals of Statistics*, *Biometrika*, and *Biometrics*, among others. Several bioinformatics tools were also developed. In particular, a differential equation modeling tool, DEDiscover, is a user-friendly software for both modelers and biomedical scientists, providing model simulation, parameter estimation and model evaluation functions. It is freely available at the UR-CBIM website https://cbim.urmc.rochester.edu/software. Extensive experimental data for model development and model validation were also generated and will be available via the NIAID/NIH immunology database, ImmPort (www.immport.org) and the UR-CBIM website.

This project has been renewed with extended scope and research activities for the next five years. In particular, the UR-CBIM aims to develop multi-level and multi-type mathematical/computational models for immune responses that include ordinary differential equation models, stochastic differential equation models, state-space models, stochastic process models, agent-based models, and network models at the cellular, protein, and genetic levels. Novel statistical methods will be developed for these complex dynamic models that are used to quantify immune responses to influenza infection and vaccination. Extensive experiments in both mice and human subjects will be performed and high-throughput experimental data at cellular, protein, and genetic levels will be collected to support development, validation, and testing of the proposed models and methods. The developed modeling techniques and statistical methods will be converted into user-friendly tools for biomedical investigators and modelers to easily use to further better understanding of immune responses and design of new experiments for discovering new immune-based therapies and vaccines against infectious agents. The collaboration and interaction

among multi-disciplinary investigators, in particular between quantitative modelers and experimental scientists, has been and will continue to be crucial for the success of this project.

The University of Rochester is one of four institutes selected to establish Centers for Modeling Immunity for Biodefense by NIH. The other three centers awarded were Duke University Medical Center, Mount Sinai School of Medicine, and the Virginia Bioinformatics Institute at Virginia Polytechnic Institute and State University. The University of Rochester's CBIM project, led by **Drs. Wu** and **Zand**, consists of five cores: a Mathematical Modeling Core, led by **Alan Perelson** and **Dr. Hongyu Miao**; a Statistics Core, led by **Dr. Wu**; a Bioinformatics Core, led by **Drs. Gregory Warnes** and **Jingming Ma**; an Immunology Core, led by **Dr. Zand**; an Administrative Core, led by **Jeanne Holden-Wiltse**; and an Education Program, led by **Drs. Hua Liang** and **Tim Mosmann**. **Dr. Alan Perelson**, a senior fellow at the Los Alamos National Lab and a world leader in immune modeling, is the subcontract PI of the UR-CBIM project.

Statisticians like **Dr. Wu** play critical roles in successful biomedical research, but rarely do they lead the large multidisciplinary research projects their work supports. This award demonstrates the importance of equally using statistical and mathematical modeling approaches, and not solely experimental methods, to make scientific discoveries. **Dr. Wu** joined the University of Rochester in 2003 and founded the interdisciplinary Division of Biomedical Modeling and Informatics at the Department of Biostatistics and Computational Biology with a goal of integrating multi-disciplinary quantitative and computational sciences for biomedical research.

Besides this Biodefense Center project, the Division, led by **Dr. Wu**, also provides statistics, mathematical modeling and bioinformatics support to several large centers or program projects at the University of Rochester Medical Center, which include the New York Influenza Center of Excellence, Clinical and Translational Sciences Institute, the Center for Biodefense of Immunocompromised Populations, Developmental Center for AIDS Research, the Rochester Prevention Research Center, Program Project of Novel Adjunctive Therapies for NeuroAIDS, and Program Project of B Cells in Health and Disease. In addition, the Division also hosts a NIH-sponsored training program in Biostatistics for HIV/AIDS Research and several investigator-initiated research projects in statistical methodologies and mathematical modeling of infectious diseases.

Pictured below: Dr. Hulin Wu, left, and Dr. Martin Zand, right

More Grant Activity

A 5-year research grant for a multicenter clinical trial RAID, evaluating a late sodium current blockade in high-risk ICD patients, has been granted to the University by NHLBI. **Dr. Jack Hall** is the Chief Statistician; **Dr. Chris Beck** and a graduate student (TBN) will also be on the project.

Department News

David Oakes participated in two meetings of the FDA Endocrinologic and Metabolic Drug Advisory Committee. The first meeting, which attracted considerable media attention, was joint with the Drug Safety and Risk Management Advisory Committee, to discuss the cardiovascular safety of rosiglitazone ("Avandia") in adults with type 2 diabetes. The second meeting, in December, concerned the weight loss drug "Contrave".

Dr. Oakes is a member of the NIH "EPIC" (Epidemiology of Cancer) Study Section and participated in review meetings in San Francisco CA, Alexandria VA, and Chicago IL

Sung Yong Park, Ph.D. a research assistant professor, along with scientists from other universities, has created a diamond-like lattice composed of gold nanoparticles and viral particles, woven together and held in place by strands of DNA. The structure - a distinctive mix of hard, metallic nanoparticles and organic viral pieces known as capsids, linked by the very stuff of life, DNA - marks a remarkable step in scientists' ability to combine an assortment of materials to create infinitesimal devices.

While people commonly think of DNA as a blueprint for life, the team used DNA instead as a tool to guide the precise positioning of tiny particles just one-millionth of a centimeter across, using DNA to chaperone the particles into the right positions to create a crystal lattice.
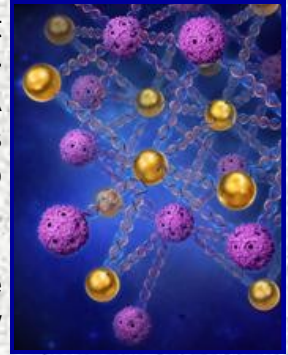
When scientists mixed the particles, out of the brew emerged a sodium thallium crystal lattice. The device "self assembled" or literally built itself.

Crystal lattice created by Sung Yong and colleagues (Illustration by Adolf Lachman)

The research adds some welcome flexibility to the toolkit that scientists have available to create nano-sized devices.

See this article in its entirety at http://www.urmc.rochester.edu/news/story/index.cfm?id=3103

Andrea Berry, MS, was hired in May 2010. She has been working with **Dr. Hyrien** on a project funded by BARDA, the Biomedical Advanced Research and Development Authority, U.S. Department of Health and Human Services. This is a collaborative effort with colleagues from the Department of Radiation Oncology at the University of Rochester Medical Center and with members of the University of Florida. She is also assisting **Drs. Peterson** and **Hyrien** in providing statistical support for projects with the Wilmot Cancer Center. Andrea received her masters degree from the Department of Biostatistics and Computational Biology in 2009.
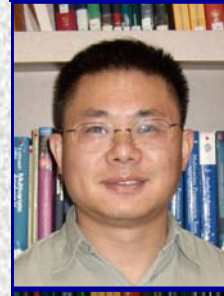
2010 Promotions and Appointments

Ollivier Hyrien, Associate Professor was granted tenure effective May 2010

Dongwen Wang, Associate Professor effective July 1. 2010

Hongqi Xue, Research Assistant Professor, effective May 1, 2010

Yinglin Xia, Research Assistant Professor effective September 1, 2010

Tanzy Love, Assistant Professor, effective June 1, 2010

Naiji Lu, Research Assistant Professor effective October 1, 2010

The Move is Almost Here

Biostatistics and Computational Biology will be moving to the **Clinical and Translational Science Building** on April 15, 2011. The building is adjacent to Helen Wood Hall, on Crittenden Boulevard. The department will share the 4th floor, approximately 39,000 sq. ft., with Heart Research. This move will unite the entire department again, consolidating our 3rd floor medical center space where Dongwen Wang and his group currently work, as well as Hulin Wu's group, which is currently offsite at the Lattimore Medical Center. The building will be LEED certified, one of the first for the University of Rochester. Leadership in Energy & Environmental Design (LEED) is an internationally recognized green building certification system, providing third-party verification that a building or community was designed and built using strategies intended to improve performance in metrics such as energy savings, water efficiency, CO_2 emissions reduction, improved indoor environmental quality, and stewardship of resources and sensitivity to their impacts. If you have the opportunity, please stop by and check out our new space.

Pictured at the left along the blackboard: Alex Pearson, Ph.D. and now M.D. student, Mike McDermott, Scott McNitt from the Heart Research Follow-Up Program, and Shawn Haarer-teacher, Wilson Magnet High School. Pictured in the middle are students from Wilson Magnet High School - Kaneesha Dukes, Cebrahil Guler-Carrasquillo, Elizabeth Haynes, Alex Huntley-Romanow, Jack Jones, Blair Lineham, Emani McCullough, Courtney Peace, Edward Schrader, Peter Stevens, Matt Taylor, and Gabriel Trevinoand Brighton High School - Ido Goldenberg and Xiao Xu. Far right is Mike Atkinson - teacher, Wilson Magnet High School.

Biostatistics Mini-Apprenticeship

The Biostatistics Mini-Apprenticeship is an outreach program developed in 2006 as a cooperative effort among the **Heart Research Follow-up Program (Scott McNitt, MS)** and the **Department of Biostatistics and Computational Biology (Michael McDermott, PhD)** at the University of Rochester, and **Wilson Magnet High School (Shawn Haarer, PhD).** The 2008 program received funding from the ASA Biometrics Section. The outreach targets mathematically talented students from Wilson High, an urban magnet school for mathematics, science, and technology in Rochester, NY, and seeks to provide them with an introduction to the interface between biostatistics and medical research. Participants also learn about career opportunities in biostatistics, bioengineering, and medicine.

The 2010 program had three phases. The first phase was an outreach day at the University of Rochester that began with an interactive lecture by cardiologist **Dr. Ilan Goldenberg** entitled "Risk of Aborted Cardiac Arrest or Sudden Cardiac Death in Subjects with Genotype-confirmed Long-QT Syndrome and Normal-Range QTc". The students then participated in small group career discussions with University researchers in biostatistics, biomedical engineering, and medicine. A brief tutorial on the process of statistical analysis was presented by Mike McDermott. He utilized a case study involving a clinical trial of multiple pharmacological treatments for attention deficit-hyperactivity disorder in children with tic disorder. At the conclusion of the first day, the students were charged with their own statistical analysis projects – to identify factors associated with heart size change in men and women and to identify factors associated with baseline QRS interval, an important predictor itself of heart failure and death. The students were given data sets obtained from actual clinical studies performed in the Heart Research Follow-up Program.

In the second phase, at Wilson High, students learned to utilize the statistical techniques presented on the outreach day using Minitab software. They were then divided into two groups to analyze each of the project data sets using both descriptive and inferential statistics. The students were motivated by the fact that they were performing new analyses using these data and would be presenting these findings to professionals in the relevant fields. In the third phase, the students returned to the University of Rochester to present their findings to an audience of biostatisticians, doctors, and medical students and a lively discussion of the analytical techniques and the medical interpretation ensued. Students were very enthusiastic about the experience and provided valuable insight for future offerings of the program.

Article Information provided by Scott McNitt and Mike McDermott

First Annual 2010 Statistics Ph.D. Student Workshop - May 21, 2010

Pictured from left to right: Mike McDermott, Graduate Program Director; Graduate Students Zhen Chen, Douglas Gunzler, Tao Lu, and Xiao Zhang; Sally Thurston, Advisor

The Department's **2nd Annual Statistics Ph.D. Student Workshop** is scheduled for May 20, 2011. The Workshop will include presentations by all Ph.D. students who have passed the Advanced Examination, but have not yet had their Proposal (Qualifying) Examination. Each student will present on his/her dissertation topic, providing some background and an update on the progress of the research. For students who have not yet identified a dissertation topic, the presentation can be material covered in a recent reading course (ideally, a *potential* dissertation topic).

The primary motivation behind this initiative is to allow students to obtain feedback on their research ideas from the entire faculty, whose perspectives may be somewhat different from that of the primary research advisor and potentially quite valuable. The Workshop will also provide additional experience for each student in preparing and delivering a presentation on a topic of his/her particular interest; this should be highly useful for developing future presentations for national meetings (e.g., ENAR, JSM) or for the Proposal Examination. Students will receive constructive feedback on their presentation from their research advisor (or, if applicable, the instructor of their reading course). It is also beneficial, of course, for faculty and other students to learn about students' planned or in-progress research.

Attendance at the Workshop is mandatory for all student presenters, other Ph.D. students, and tenure-track faculty. Other members of the department are also welcome.

From left to right: David Oakes, Setta Odoroff and Raymond J. Carroll

2010 Charles L. Odoroff Memorial Lecture

On April 16, 2010, **Raymond J. Carroll, Ph.D.**, Distinguished Professor of Statistics, Nutrition and Toxicology, with the Department of Statistics, Director at the Center for Statistical Bioinformatics, and Deputy Director with the Institute for Applied Mathematical and Computational Science at Texas A&M University gave a lecture on *"Robust Powerful Methods for Understanding Gene-Environment Interactions"*. This was the twenty-second lecture in the series.

The **2010 Spring Colloquium Series** included the following speakers:

Alexander Tsodikov, Ph.D., Professor of Biostatistics at the University of Michigan, lectured on *"Modeling Treatment Efficacy Under Screening"* (March 11, 2010)

Debajyoti Sinha, Ph.D., Professor and Chair of the Department of Statistics at Florida State University, who lectured on *"Median Regression in Survival Analysis via Transform-Both-Sides Model"* (April 29, 2010)

Laurel A. Beckett, Ph.D., Professor and Chief with the Division of Biostatistics, Vice Chair in the Department of Public Health Sciences at the University of California at Davis, who lectured on *"Statistical Challenges*

in Identifying Biomarkers for Alzheimer's Disease: Insights from the Alzheimer's Disease Neuroimaging Initiative" (May 20, 2010)

From left to right: David Oakes, Nina Yakovlev and Michael Kosorok

2010 Yakovlev Colloquium

To honor Dr. Andrei Yakovlev's major contributions to the department, our first colloquium each academic year is dedicated to his memory. On October 28, 2010, **Michael R. Kosorok, Ph.D.**, Professor and Chair of Biostatistics at the University of North Carolina at Chapel Hill, gave a lecture on *"Reinforcement Learning, Clinical Trials and Personalized Medicine"* .

The **2010 Fall Colloquium Series** consisted of the following speakers:

Ping Ma, Ph.D., Assistant Professor of Statistics in the Department of Statistics at the University of Illinois at Urbana-Champaign, lectured on *"Nonparametric Modeling of Next Generation Sequencing Data"* (October 28, 2010)

Jerry Lawless, Ph.D., Distinguished Professor Emeritus with the Department of Statistics and Actuarial Science at the University of Waterloo, lectured on *"Profile Likelihood and Semiparametric Models, with Application to Multivariate Survival Analysis"* (November 4, 2010)

Nick Holford, Ph.D., Professor with the Department of Pharmacology and Clinical Pharmacology at the University of Auckland, New Zealand, lectured on *"Delaying Time-to-Event in Parkinson's Disease"* *(November 11, 2010)*

Hongyu Zhao, Ph.D., Professor of Public Health with the Department of Genetics at Yale University, lectured on *"Risk Prediction Models from Genome Wide Association Data"* *(December 2, 2010)*

Bradley P. Carlin, Ph.D., Professor and Head of the Division of Biostatistics at the University of Minnesota School of Public Health, lectured on *"Hierarchical Commensurate and Power Prior Models for Adaptive Incorporation of Historical Information in Clinical Trials"* *(December 7, 2010)*

Upcoming Speakers for the 2011 Spring Colloquium Series

February 17, 2011
John Kolassa, Ph.D.
Rutgers University

March 10, 2011
Gong Tang, Ph.D.
University of Pittsburgh

March 24, 2011
Xueya Cai
University of Iowa

May 12, 2011
Mary Sammel, Ph.D.
University of Pennsylvania

May 26, 2011
2011 Charles L. Odoroff Memorial Lecture
Amita Manatunga, Ph.D.
Emory University
Rollins School of Public Health

2010 Commencement Ceremony

Ph.D. diplomas were awarded to three graduate students from Biostatistics on May 15, 2010.

Qin Yu (top picture) with advisor, **Xin Tu, Ph.D.** Qin is presently working as a Research Associate at the University of Pennsylvania.

Haiyan Su (middle picture) with advisor, **Hua Liang, Ph.D.** Haiyan is an Assistant Professor in the Department of Mathematical Sciences at Montclair State University.

Abbie Stokes-Riner (bottom picture) with advisor, **Sally Thurston, Ph.D.** Abbie is presently working in the private sector at EMMES Corporation as a biostatistician.

Congratulations to all on your hard work!!!

Photographs provided by Wei Liang

Student News

On June 23rd, **Hui Zhang** successfully defended his thesis, "*Distribution-free Models for Latent Population Mixtures*" under the advisement of **Professor Xin Tu.**

Hui was also honored as a recipient of the Chinese Government Award for Outstanding Students Abroad. The award included a $5,000 US prize and was awarded to Hui at the end of June 2010 by the Consulate-General of People's Republic of China in New York City.

Hui Zhang, Ph.D., now holds a position as an Assistant Member in the Department of Biostatistics at **St. Jude Children's Research Hospital** in Tennessee.

Saria Awadalla had a successful thesis proposal on May 26, 2010. His advisors are **Govind Mudholkar, Ph.D.** and **Mike McDermott, Ph.D.**

Hui Zhang is pictured cutting his celebration cake, with his advisor **Xin Tu** observing from the background (right).
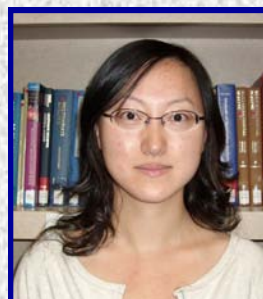
On December 20th, **Miranda Lynch** (pictured left, with her advisor, **Sally Thurston**) successfully defended her thesis, *"Estimation, model checking and diagnostics, and identifiability in finite mixture models for point mass data: Methods in a Bayesian framework"*.

Miranda Lynch, Ph.D. is now a postdoctoral research fellow at the **Harvard School of Public Health** in Boston, MA.

Xiang Liu had a successful thesis proposal on June 18, 2010. Her advisor is **Hua Liang, Ph.D.**

Student News - continued

Jason Lacombe had a successful thesis proposal on September 16, 2010. His advisor is **Anthony Almudevar, Ph.D.**

Tian Chen did her undergraduate work at the University of Nankai, and received her master's from the University of Toledo. Tian's hometown is Sichuan, China
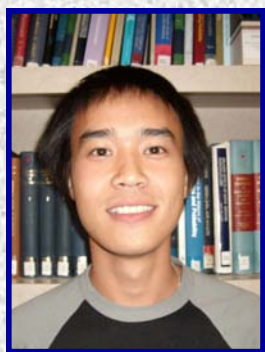
Tao Lu, also had a successful thesis proposal on October 13, 2010. His advisor is **Hulin Wu, Ph.D.**

Jason Morrissette did his undergraduate work here at the University of Rochester (River Campus). Jason is a native Rochesterian from Gates, New York.

The new 2010-2011 academic year brought 5 doctoral students and 1 master's student from different parts of the world.

Changming Xia, a.k.a. Sherman, earned his BS in Telecommunication Engineering at the Harbin Institute of Technology in China, and MS in Applied and Computational Mathematics from the University of Minnesota-Duluth. Changming's hometown is Foshan, China.

Fei Ma finished her undergraduate work at the Shanghai University of Finance and Economics before coming to the U of R. Fei's hometown is Wuhan, China.

Van Tran received her bachelor's degree from the University of Rochester (River Campus). Van's hometown is Syracuse, New York.

Ziji Yu is a master's student who received her bachelor's degree at Remin University of China. Ziji's hometown is Daqing, Heilongjiang Province, China

2010 Family Winter Celebration

The Department celebrated with family at Clover Lanes in Pittsford, NY with a winter bowling party on Friday, January 29th.

Over 100 people attended the event, and from the smiling faces, a good time was had by all.

The 2011 Winter Celebration will be February 11, 2011.

2010 Annual Family Picnic

Our picnic was held on Friday, July 9th at Pineway Ponds Park in Spencerport, N.Y. This year the weather was not on our side as the torrential rain came as soon as the food arrived, and it rained off and on for most of the day. Everyone enjoyed each other's company and conversation. The kids had a great time playing in the rain.

The 2011 Family Picnic will be announced at a later date.

News from Around the World...

We congratulate **Dr. Nancy Geller** on her election as President of the American Statistical Association! Her term of office began January 1, 2011. Nancy was a member of the Department of Statistics faculty here from 1970-1972, while completing her PhD at Case Western Reserve University. She is now Director of the Office of Biostatistics Research at the National Heart, Lung and Blood Institute of NIH, and has amassed an exemplary record of research and administrative contributions over the years. Congratulations on all of the above!

Dr. Siddhartha Dalal has been appointed Chief Technology Officer (CTO) at the RAND Corporation in Santa Monica (CA). Sid was in the first class of graduate students in our Department of Statistics, completing his PhD in 1976, with an MBA in 1973 along the way. Before going to RAND in 2007, he served for 5 years as a vice president at Xerox here in Rochester, overseeing Xerox's worldwide research on Imaging and Software in Rochester, Palo Alto and Los Angeles. Check out his recent paper in the Annals of Applied Statistics (Vol. 4, 2010) on a Bayesian approach to detection of radioactive material entering ports.

At a conference last summer in Seattle, honoring the 65th birthday of **Professor Jon Wellner,** Dr. Wellner was knighted by a representative of the Queen of the Netherlands to recognize his contributions to the development of mathematical statistics in the Netherlands. Congratulations, Jon! Jon was on the UR faculty from 1975 to 1983. Participating in the Conference were scholars from around the world (including Jack Hall).

Professor Wei-Min Huang has been reappointed as Chair of the Department of Mathematics at Lehigh University for another term of 3 years. Wei-Min completed his PhD in Statistics here in 1982, and has been on the Lehigh faculty ever since, amassing a fine record of statistical research, teaching and student supervision.

Dr. Yan Ma, a member of the CTSC Research Design and Biostatistics Core Team at Weill Cornell Medical College has been selected to receive the Statistics in Epidemiology Young Investigator Award by the American Statistical Association (ASA).

Dr. Ma's winning paper, "Inferences for Kappas for Longitudinal Data," was supported by the Clinical Translational Science Center (CTSC) (UL1-RR024996). The paper proposed a non-parametric method for estimating Kappa coefficient, within a longitudinal data setting in the presence of missing data.

Yan Ma received his Ph.D. from the University of Rochester in 2008 under the advisement of **Dr. Xin Tu**.

See this article in its entirety at http://www.weill.cornell.edu/ctsc/news/resources/eNewsLetter_Fall_2010.pdf#page=3

We are saddened to report the recent death of Professor **Edward Dudewicz.** Ed was in the first group of faculty at the UR Department of Statistics, serving from 1968 to 1975, as Instructor while completing his PhD at Cornell University and then as Assistant Professor. He had a long and distinguished career at Syracuse University.