Mathematical Biosciences Institute
at The Ohio State University

photo by Steve Turek

Ecology & Evolution

2005-2006

The MBI receives major funding from the National Science Foundation
Division of Mathematical Sciences and is supported by the Ohio State University.
The Mathematical Biosciences Institute adheres to the AA/EOE quidelines.

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Director's Letter

The Mathematical Biosciences Institute at the Ohio State University was created in 2002 in order to provide a national forum in research and education for the mathematical biosciences. Funded by the Division of Mathematical Sciences of the National Science Foundation, the Institute's goals are to catalyze interactions between the mathematical and biological sciences, and to nurture a nationwide community of scholars in this emerging field. The MBI aims to reinforce and build upon existing research efforts in mathematical biosciences, and quicken intellectual growth in this area.

The MBI runs "Emphasis Year" programs, concentrating on a broad range of topics in one area of bioscience, with six to eight one-week workshops preceded by tutorials. In the summer, the MBI runs educational programs based on tutorials and team projects led by MBI postdoctoral fellows. Occasional "Current Topics" workshops introduce mathematical scientists to new opportunities for research. The topics of the first three emphasis years were Mathematical Neurosciences; Mathematical Modeling of Cell Processes; and Genomics, Proteomics, and Bioinformatics. This year was devoted to Ecology and Evolution.

Ecology and evolutionary biology have historically been two of the areas of biology which have benefited most from, and made use of, mathematical methods. Many distinguished mathematical biologists have contributed to these areas, and their efforts have illuminated much of ecological and evolutionary theory over the past century. The objective of this special year was to focus on specialized areas that offer particularly challenging mathematical problems that are relatively unexplored and are of potentially great interest to observational biologists. Thus, an underlying goal of the proposed activities was to maintain direct connections to observable biology.

The year began with a one week tutorial on tree reconstruction and coalescence theory. It was followed by a workshop on phylogeography and phylogenetics, topics which will be critical in studying dispersal distances, mating systems, pathogen history, and local adaptations. Another shorter workshop was devoted to phylogenetic analysis of large databases. The Fall Quarter included a workshop on self-organization in evolution, focused on the transition from artificial to living cells, evaluation of neural networks, and evolution of biological complexity.

The winter program included a one-week tutorial on reaction-diffusion models. In a workshop on spatial heterogeneity, models were presented to address the complexity of evolutionary dynamics as driven by ecological and coevolutionary interaction in spatially explicit context. Another workshop on spatial ecology dealt with the effects of spatial factors on population structure.

The spring program featured workshops on microbial ecology and global ecology. Another workshop dealt with the difficult issue of uncertainty in ecological analysis: How to accurately account for multiple sources of uncertainty.

As in the previous year, the MBI postdoctoral fellows organized a special workshop for young researchers in mathematics biosciences. Participants included 45 young researchers from all over the country. This exciting workshop included poster presentations by the young researchers, as well as group discussions. There are currently 12 postdoctoral fellows at the MBI, each having two mentors, one from the mathematical sciences and another from the biosciences. Five of the postdoctoral fellows have graduated this year, and took positions in research universities and in public and private industry.

This year the MBI began a public lecture series. The first three talks were related to workshops themes. The topics were:

- The Global Loss of Top Predators in the Ocean: Consequences of a World Without Sharks, Tuna, and Great Fish
- Blind Dating: The Secret Life of Pelagic Copepods
- Global Warming: Why the Skeptics Are Wrong

Another new feature introduced this year is a two-week summer program for undergraduates. As in the ongoing summer program for graduate students, this program includes short tutorials and team projects, and visits to biological labs. Several of the undergraduates remained at the MBI for the entire summer to work in depth on the research project of their team.

This document provides a summary of events and talks that took place in the fourth year of the MBI. Further details can be found on the MBI website http://mbi.osu.edu.

Avner Friedman
Director

Mission and Goals

The explosion of research in the life sciences has created the need for new mathematical theories, statistical methods, and computational algorithms with which to draw knowledge from the rapidly accumulating data. The Mathematical Biosciences Institute catalyzes interactions between the biological, medical, and mathematical sciences through vigorous programs of research and education and nurtures a nationwide community of scholars in this emerging new field.

The mission of the MBI is:

- To develop mathematical theories, statistical methods, and computational algorithms for the solution of fundamental problems in the biosciences;
- To involve mathematical scientists and bioscientists in the solutions of these problems; and
- To nurture a community of scholars through education and support of students and researchers in mathematical biosciences.

Participants in the first Summer Program for Undergraduates in Mathematical Biology held July 5-17, 2006.

Corporate Members

The MBI encourages involvement from those in private industry. The institute offers incentives to pharmaceutical and bioengineering companies interested in becoming a corporate member.

Membership benefits include:

- Regular visits by MBI Directors to identify problems and topics of interest, where mathematical sciences could be helpful;
- Follow-up to these problems by institute researchers;
- An invitation to present industrial challenges and problems to MBI audiences and to participate in MBI Programs and workshops.

Current Corporate Members:

- Pfizer
- GlaxoSmithKline

Participants discussing projects in the Summer Undergraduate Program in Mathematical Biology.

Institute Partners

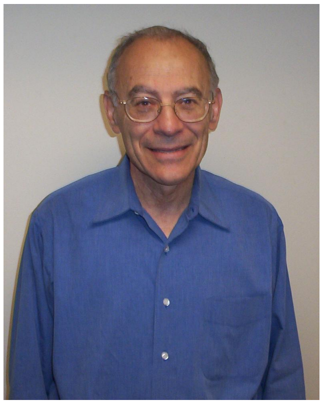
The MBI Institute Partners Program subsidizes the travel and local expenses of IP members and faculty, postdoctoral fellows, and students to allow their participation in research and education programs at the MBI; for details see the MBI website http://mbi.osu.edu.

Current Institute Partners

Arizona State University
Case Western Reserve University
Drexel University
Florida State University
Indiana University-Purdue University Indianapolis
Iowa State University
Michigan State University
New Jersey Institute of Technology
Ohio University
University of California at Irvine
University of Cincinnati
University of Georgia
University of Iowa
University of Maryland, Baltimore County
University of Minnesota
Vanderbilt University

Summer Programs participants preparing for group projects.

Directors



The director provides the scientific leadership, promotes the institution's mission and goals, and is responsible for the overall management and resource development of the institute. The director reports to the Board of Governors.

Avner Friedman, MBI Director

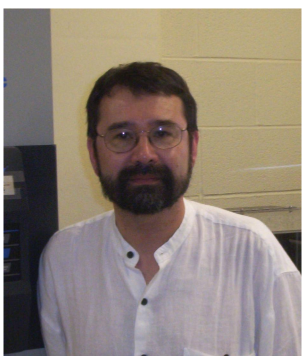
The senior associate director acts as the director during the director's absence, and designs and implements initiatives consistent with the MBI mission.

David Terman, MBI Senior Associate Director

Libby Marschall, Evolution, Ecology, and Organismal Biology, The Ohio State University Associate Director

Three associate directors provide scientific advice and support to the director. Along with the director, they visit bioscience laboratories in the public and private sectors in order to initiate and nurture interactions with the institute. Associate Director Dennis Pearl is responsible for the education programs, as well as the evaluation process. Associate Director Andrej Rotter provides leadership for the Current Topics Workshops. Associate Director Libby Marschall works with the Director on diversity issues. The Associate Directors together with the Senior Associate Director are responsible for arranging the mentoring program for postdoctoral fellows.

Dennis Pearl, Department of Statistics, The Ohio State University Associate Director



Andrej Rotter, Department of Pharmacology, The Ohio State University Associate Director

The Assistant Director Tony Nance is a full time staff member with duties that include oversight of the day-to-day operation of the MBI offices and supervision of the institute staff.

Tony Nance, MBI Assistant Director

Staff

Nikki Betts, Administrative Associate: Manages all human resources and financial activity in the MBI, including visa, travel, and reimbursement related activities. She also helps with program and reporting activities.

Stella Cornett, Program Assistant: Manages the web site; produces grant proposals and reports; produces print series for technical reports and works with publishers and authors on MBI publications; and receives participant abstracts and presentation materials and places them on the web.

Rebecca Martin, Office Associate: Provides direct office support for the Director; serves as primary point of contact to all outside the MBI; sends letters of invitation to all workshop and tutorial participants.

Matt Thompson, Program Assistant: Assists in fiscal processing, registration, human resources, promotion and advertising, including creation and distribution of MBI posters, brochures, and flyers; responsible for information given to all visitors.

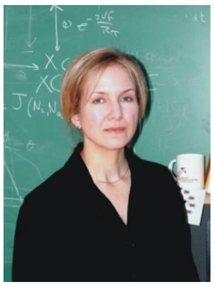
Michael Siroskey, Systems Manager: Responsible for all technology aspects of the MBI, including maintaining and upgrading servers, desktop and laptop machines; handles hardware and software evaluation and procurement decisions; responsible for presentation and telecommunication facilities; provides support on space renovation project; and supervises web activity.

Dhruv Kaura, Student Worker: Provides clerical support on MBI annual programs and works closely with Program Assistant Matt Thompson.

MBI Postdoctoral Fellows

Postdoctoral fellows fall into two support categories: Supported at 100 percent by the MBI or split 50/50 percent by the MBI and another bioscience organization. Postdoctoral fellows sponsored by a specific organization spend 50 percent of their time on research suggested by the sponsor. All postdocs are provided with two mentors: one from the mathematical, statistical, and computational sciences, and another from one of the bioscience departments at The Ohio State University. Long-term visitors may also serve as mentors. More details are available in the *MBI Postdoctoral Research Program Handbook* on the MBI website.

Cohort of 2003



Janet Best (Department of Mathematics, Cornell University). Janet has accepted a faculty position in the Department of Mathematics at the Ohio State University and will remain a local affiliate of the MBI. Her current focus is on mathematical models of the sleep/wake cycle, and modeling the pulsatile release of reproductive hormones and its onset at puberty.

While at the MBI, she has worked closely with experimental biologists, which has refined her ability to interpret experimental data. She has developed mathematical approaches for modeling some neuronal computations and has advanced the mathematical techniques for analyzing these often complex models.

The sleep/wake model will be applicable, ultimately, not only by doctors treating sleep disorders, but also by individuals who want to understand and to manage their own sleep/wake habits. Janet plans to work with others on developing a clinically applicable version of the reproductive hormone model. She also looks forward to involving more students in these and other research projects, and to expand the mathematical biology curriculum at OSU.

Pranay Goel (Department of Mathematics, University of Pittsburgh). Pranay has been hired on as a research fellow at NIH/NIDDK. With Arthur Sherman, he will be working on mathematical modeling associated with diabetes. Currently, he is working with Erin Higgins and James Sneyd on calcium transients in the cardiac myocyte during Excitation-Contraction coupling. He plans to continue work on important problems in biology using mathematics, especially those that involve human diseases.

Sookkyung Lim (Courant Institute of Mathematical Sciences, New York University). Sookkyung Lim has accepted a position in the Department of Mathematics at University of Cincinnati. Presently, she is working on valveless pumping, dynamics of a circular rod (with twist and bend in fluid), and aortic aneurysms.

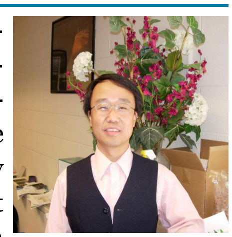
She has gained much knowledge at the MBI, including: understanding in mathematical biology through workshops, seminars, and tutorials; how to organize workshops and seminars; and how to communicate with scientists from non-mathematical sciences. She has had opportunities to meet leading researchers in mathematical biology and has developed a collaboration with people from the biological sciences.

In her future work, Sookkyung hopes to develop curricula in the area of interdisciplinary research (such as mathematical biology and biophysics), simulate flagellar motion of E. coli, and investigate zebrafish ciliary motion.

Cohort of 2004

Diego Pol (Department of Earth and Environmental Sciences, Columbia University). Diego has been hired to a federally funded tenure track position at the Museo Paleontologico Egidio Feruglio in Argentina. He has several projects recently completed or in the works, including phylogenetic analysis of emerging infectious diseases and research on genetic algorithms for tree searches in phylogenetics. Using phylogenetic methodology, he and collaborators were able to prove that Dinosaurs lived not only in North America but also in South America. While at the MBI he helped organize two workshops (one at OSU and one in Brazil). He published several papers in phylogenetics or in which he applied phylogenetic analysis to other fields in genomics.

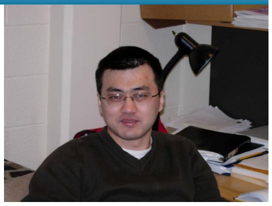
Mike Stubna (Cornell University). Mike was hired as an Instructor in Mathematics at Penn State McKeesport. His research interest is in the application of dynamical systems modeling and analysis to physical and biological systems. Research topics have included cardiac electrophysiology, QT interval regulation, electrical power grid dynamics, and parametrically forced mechanical systems.



Jianjun (Paul) Tian (Department of Mathematics, University of California, Riverside). Paul has been involved in many aspects of biology and medicine, namely: the quantitative study of brain tumor growth, virotherapy, radiotherapy, and chemotherapy by using partial differential equations; the quantitative study of disease ecology, particularly avian influenza virus, by using ODEs and Markov processes; genetic models and colored coalescent theory by using stochastic processes; the application of evolution algebras in genetics; immunotherapy of tumors by using delay ODEs; tumor data analysis by using statistical algorithms; and modeling of niche signals of neural stem cells and brain tumor genesis. His current research is in mathematical modeling of niche signals of neural stem cells and brain tumor genesis. His goal is to advance understanding of neural stem cell behavior; to provide insight into the origin of brain tumors; and to provide a rationale for neural stem cell treatment of degenerative diseases in the central nervous system.

Zailong Wang (Department of Statistics, University of California, Davis). Zailong was recently hired by Novartis Inc. at East Hanover, N.J. as Senior Statistician. His research interests include: biostatistics, bioinformatics, data mining and machine learning. Currently, he focused on applying Bayesian approach and Markov Chain Monte Carlo (MCMC) methodology to gene expression data analysis such as microarray data, ChIP-on-chip data, and SAGE (Serial Analysis of Gene Expression) library data. The Bayesian Hierarchical models and reversible jump MCMC proposals have been developed for gene expression analysis.

Jin Zhou (Department of Statistics, University of Georgia). Jin Zhou's current research interests include microRNA target prediction, methods on rank aggregation, time series analysis in queueing system, and stochastic differential equation. His future projects include microRNA's role in human cancer. Specifically, he wants to know the answer for such questions: What's microRNA's expression signature on NCI60 cell lines of human cancer, and what is the relationship of microRNA's expression and mRNA's expression? Another project he is working on is the stochastic differential equation models for the spread of influenza virus in poultry and humans.



Cohort of 2005

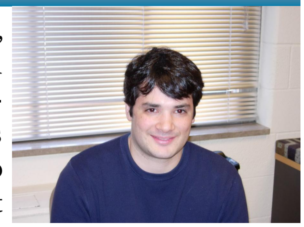
Marko Djordjevic (Department of Physics, Columbia University). Marko's research interests are broadly in the area of computational biology and bioinformatics. More specifically, he is interested to computationally study regulation of gene expression by using ideas and methods from statistical physics. In addition to analyzing experimental data, his theoretical/ computational research is also aimed at contributing to the experimental design. To accomplish a close interaction of theory with experiment, he is intensively collaborating with experimental biology labs.

His current research is mainly directed to transcription regulation in higher eukaryotes, and aims to address the following questions: How to reliably infer protein-DNA interaction parameters and predict direct target genes of TFs? How RNA polymerase (an enzyme that transcribes genes) initiates transcription and how to accurately predict transcription start sites in genome? What are (some) principal limits in accuracy of the computational algorithms and high-throughput experimental techniques that are used to study transcription regulation?

German Enciso (Department of Mathematics, Rutgers University). While German is currently considering a more applied approach to mathematical biology, his dissertation research consisted of the study of certain abstract dynamical systems called monotone systems, which are associated with positive feedback and have strong stability properties. Using ideas from control theory, some non-monotone systems were studied using ideas from monotone systems theory. Applications were given to delay and reaction diffusion equations in molecular biology.

Paula Grajdeanu (Department of Applied Mathematics, University of Durham, England). Paula is interested in many aspects of mathematical biology including renal physiology; cell metabolism; immunology; and formulating mathematical models for various clinical problems. She believes that Math-Bio is a fascinating subject and she would like to be one who will lead other students in understanding the beauty, relevance, and importance of mathematics applied in real life problems.

Andrew Nevai (Department of Mathematics, University of California, Los Angeles). Andrew is interested in many aspects of mathematical ecology including the theory of competition for resources; species persistence and permanence within ecological communities; the dynamics of spatially (or otherwise) structured populations; individual and group foraging theory; behavior; and formulating ecological models that make use of mechanistic reasoning and principles.



So far at the MBI, he has collaborated with Yuan Lou (OSU), Winifried Just (Ohio University), Tom Waite (OSU), Kevin Passino (OSU), Ben Bolker (University of Florida), Linda Allen (Texas Tech University), and Partha Srinivasan (MBI).

Richard Schugart (Department of Mathematics, North Carolina State University). Richard's research interests include mathematical modeling and scientific computing as applied to problems in wound healing and cartilage mechanics. His dissertation work included two problems in cartilage mechanics and is motivated by the need to quantify differences between normal and osteoarthritic mechanical and physico-chemical states in cartilage. The first problem involved the formulation and analysis of mathematical models for osmotically-induced volume change in articular cartilage cells and chondrons, which is the functional cell-matrix unit in cartilage. The second problem was the development of an accelerated numerical method for the continuous spectrum biphasic poroviscoelastic (BPVE) model of articular cartilage deformation. The research was directed under the supervision of his dissertation adviser, Dr. Mansoor Haider, and was in collaboration with the Orthopaedic Bioengineering Lab at the Duke University Medical Center. His current research is on wound healing, cartilage healing, and dialysis.

Partha Srinivasan (Department of Mathematics, Florida State University). Partha is working with Rolf Barth (Integrated Biomedical Science Graduate Program, OSU) in estimating the survival time of rats with melanoma metastatic to the brain after they have been treated with Boron Neutron Capture Therapy.

In collaboration with the groups of Philip Grandinetti (Dept. of Chemistry, OSU) and Martin Caffrey (Dept. of Biophysics, Biochemistry and Chemistry, OSU), he is working on understanding the structure and dynamics of proteins in the cubic phase using solid state NMR. The measurement of the dipolar coupling between a half-integer quadrupolar nuclei and a spin-1/2 nuclei can lead to a better understanding of the structure and dynamics of proteins. He is currently working with Philip Grandinetti (Dept. of Chemistry, OSU) and Domique Massiot (CRMHT-Orléans, France) on designing experiments that will allow for the measurement of this dipolar coupling term.

Brandilyn Stigler (Department of Mathematics, Virginia Tech). Brandilyn's research involves the development of a mathematical framework for the reverse-engineering of biochemical systems. The models used in this work are time- and state-discrete finite dynamical systems, described by polynomial functions over a finite field. This novel approach, rooted in computational algebra, uses Groebner-basis techniques to build the set of all discrete models that fit time series data and to select minimal models from this set. The method has been specifically designed for experimental data from biochemical networks, where the data may take the form of time series of mRNA, protein, and/or metabolite concentrations. This work is currently being applied to an oxidative stress response network in yeast.

Board of Governors

The Board consists of 13 internationally recognized mathematical scientists and bioscience researchers from academia and industry. The Board meets annually to review the institute programs, to suggest and decide on new annual programs, and to give advice regarding programmatic goals and the general management of the institute.

- Reka Albert - Department of Physics, Pennsylvania State University
- Herb Bresler - Department of Health and Life Science, Battelle Memorial Institute, Columbus, OH
- Leah Edelstein-Keshet - Department of Mathematics, University of British Columbia
- Lisa Fauci - Department of Mathematics, Tulane University
- Louis Gross - Professor of Ecology and Evolutionary Biology, The University of Tennessee
- Sorin Istrail - Center for Computational Moleclar Biology, Computer Science Department, Brown University
- Kirk Jordan - IBM Computational Biology Center
- Jim Keener - Departments of Mathematics and Bioengineering, University of Utah
- Philip Maini - Centre for Mathematical Biology, Mathematical Institute, University of Oxford
- Claudia Neuhauser - Professor of Ecology, Evolution, and Behavior, University of Minnesota
- Terry Therneau - Division of Biostatistics, Mayo Clinic College of Medicine, Rochester
- Frank Tobin - Scientific Computing & Mathematical Modeling, GlaxoSmithKline
- Raimond L. Winslow - Center for Cardiovascular Bioinformatics and Modeling, Whitaker Biomedical Engineering Institute, Department of Biomedical Engineering, The Johns Hopkins University School of Medicine and Whiting School of Engineering

Emphasis Year Scientific Advisory Committee 2005-2006

The Emphasis Year Scientific Advisory Committee reviews the emphasis year proposal as they evolve and offers suggestions throughout the development of the emphasis year. A new committees is appointed for each emphasis year program.

- Frank Berendse, Natuurbeheer en Plantenecologie
- Chris Cosner, Department of Mathematics, University of Miami
- Marcus W. Feldman, Department of Biological Sciences, Stanford University
- John Harte, Department of Environmental Science, Policy, & Management, Ecosystem Sciences, University of California
- Alan Hastings, Department of Environmental Science and Policy, University of California
- Suzanne Lenhart, Mathematics Department, University of Tennessee
- Simon Levine, Department of Ecology and Evolutionary Biology, Princeton University
- Peg Riley, Osborn Memorial Laboratories, Department of Ecology and Evolutionary Biology, Yale University
- Montgomery Slatkin, Department of Integrative Biology, University of California, Berkeley
- Gunter Wagner, Department of Ecology and Evolutionary Biology, Yale University

Local Scientific Advisory Committee

The Local Scientific Advisory Committee helps identify current topics workshops, suggest ideas for future emphasis programs, and potential mentors for postdoctoral fellows.

Sudha Agarwal	Department of Oral Biology
Irina Artsimovitch	Department of Microbiology
Michael Beattie	Department of Neuroscience
Laura Bohn	Department of Pharmacology and Psychiatry
Ralf Bundschuh	Department of Physics
Helen Chamberlin	Department of Molecular Genetics
Albert de la Chapelle	Human Cancer Genetics
Meg Daly	Department of Evolution, Ecology, and Organismal Biology
Andrea Doseff	Heart and Lung Research Institute, Department of Molecular Genetics, and Department of Internal Medicine
Martin Feinberg	Department of Chemical Engineering
Paul Fuerst	Department of Evolution, Ecology, and Organismal Biology
Erich Grotewold	Department of Plant Biology
Charles R. Hille	Department of Molecular and Cellular Biochemistry
Daniel Janies	Department of Biomedical Informatics
Doug Kniss	Department of Obstetrics and Gynecology
Mario Lauria	Department of Computer Science & Engineering
Stanley Lemeshow	Dean School of Public Health, Center for Biostatistics
Gustavo Leone	Department of Molecular Virology, Immunology, and Medical Genetics
Shili Lin	Department of Statistics
Elizabeth Marschall	Department of Evolution, Ecology, and Organismal Biology
Deborah Parris	Department of Molecular Virology
Dennis Pearl	Department of Statistics
John Reeve	Department of Microbiology
Andrej Rotter	Department of Pharmacology
Wolfgang Sadee	Department of Pharmacology
Joel Saltz	Department of Biomedical Informatics
Larry S. Schlesinger	Division of Infectious Diseases and Center for Microbial Interface Biology
Petra Schmalbrock	Department of Radiology
Amanda Simcox	Department of Molecular Genetics
Don Stredney	Biomedical Applications, Ohio Supercomputer Center
David Terman	Department of Mathematics

Program Participation 2005-2006

Program	# Participants
Tree Reconstruction and Coalescence Theory, September 7-9, 12-13, 2005	27
Workshop 1: Phylogeography and Phylogenetics, September 26-30, 2005	74
Workshop 2: Aspects of Self-Organization in Evolution, November 14-18, 2005	62
Current Topics Workshop: The Problems of Phylogenetic Analysis of Large Datasets, December 1-2, 2005	68
Workshop 3: Spatial Heterogeneity in Biotic and Abiotic Environment Effects on Species Ranges, Coevolution, and Speciation, February 6-10, 2006	89
Tutorial on Reaction-Diffusion Models, March 9-10, 2006	30
Workshop 4: Spatial Ecology, March 13-17, 2006	72
Second Young Researchers Workshop in Mathematical Biology, March 27-30, 2006	73
Workshop 5: Uncertainty in Ecological Analysis, April 3-6, 2006	99
Workshop 6: Microbial Ecology, May 15-19, 2006	53
Workshop 7: Global Ecology, June 26-30, 2006	43
Summer Undergraduate Program, July 5-17, 2006	13
Summer Education Program, July 17-August 4, 2006	31
Total	***604***
Long Term Visitors:	
4 weeks - 3 months	5
3 months - 1 year	12
Total	***17***

Long Term Visitors

Visitors 2005-2006	
Baltazar Aguda	Mathematical Biosciences Institute, The Ohio State University
Linda Allen	Department of Mathematics, Texas Tech University
Ben Bolker	Department of Zoology, University of Florida
Catherine Calder	Department of Statistics, The Ohio State University
Noel Cressie	Department of Statistics, The Ohio State University
Steve Deckelman	Department of Mathematics, Statistics, and Computer Sciences; University of Wisconsin at Stout
Jennifer R. Galovich	Department of Mathematics, St. John's University, Minnesota
Bo Guan	Department of Mathematics, The Ohio State University
Bei Hu	Department of Mathematics, University of Notre Dame
Winfried Just	Department of Mathematics, Ohio University
Yang Kuang	Department of Mathematics and Statistics, Arizona State University
Shili Lin	Department of Statistics, The Ohio State University
Irakli Loladze	Department of Mathematics, University of Nebraska-Lincoln
Yuan Lou	Department of Mathematics, The Ohio State University
Guillermo Reyes	Escuela Politecnica Superior, Universidad Carlos III de Madrid, Spain
Laura Salter Kubatko	Department of Statistics, University of New Mexico
Rui Zhao	Department of Mathematics, University of California, Irvine

Anticipated Visitors 2006-2007	
Baltazar Aguda	Mathematical Biosciences Institute, The Ohio State University
Janet Best	Department of Mathematics, The Ohio State University
Linda Chen	Department of Mathematics, The Ohio State University
Adela Comanici	Department of Mathematics, University of Houston
Gregg Hartvigsen	Department of Biology, SUNY
Tailen Hsing	Department of Statistics, The Ohio State University
Jason Hsu	Department of Statistics, The Ohio State University
Chiu-Yen Kao	Department of Mathematics, The Ohio State University
Shannon LaDeau	Smithsonian Migratory Bird Center, National Zoological Center
Shili Lin	Department of Statistics, The Ohio State University
Yuan Lou	Department of Mathematics, The Ohio State University
Bart Ng	Department of Mathematical Sciences, Indiana University-Purdue University Indianapolis
Yvonne Stokes	School of Mathematical Sciences, University of Adelaide
Joe Verducci	Department of Statistics, The Ohio State University
Linghai Zhang	Department of Mathematics, Lehigh University

Summary of the Year in Ecology and Evolution 2005-2006

Ecology and evolutionary biology have historically been two of the areas of biology which have most benefited from, and made use of, mathematical methods. Many distinguished mathematical biologists have contributed to these areas, and their efforts have illuminated much of ecological and evolutionary theory over the past century. An objective of this special year is to focus on specialized areas that offer particularly challenging mathematical problems, which are relatively unexplored and are of potentially great interest to observational biologists. Thus, an underlying goal of the proposed activities is to maintain direct connections to observable biology.

One thread of connection between the various proposed activities concerns spatial aspects of natural systems. Central questions about the history and structure of biological systems are affected by spatial variation. Additionally, numerous problems, which have great public impact, necessarily involve the spatial heterogeneity of biological systems, both those occurring through natural processes and those deriving from human actions. Conservation biology, biodiversity, harvest planning, invasive species control, and wildlife management are just a few of the applications that utilize mathematical methods to address major public policy issues. These applied areas rely greatly upon general ecological and evolutionary genetics theory. Determining how natural systems are affected by interactions of space and time leads to problems that require mathematical approaches. Although a large body of mathematical literature has developed over the past several decades dealing with spatio-temporal interactions, there are still many biologically important questions that require new mathematical approaches and would benefit from close collaborations between ecologists, evolutionary biologists, and mathematicians.

Organizing Committee

- Chris Adami, Digital Life Laboratory, California Institute of Technology and Keck Graduate Institute of Applied Life Science
- Sergey Gavrilets, Department of Ecology and Evolutionary Biology, The Institute for Environmental Modeling, Department of Mathematics, University of Tennessee
- Lou Gross, Department of Ecology and Evolutionary Biology, The Institute for Environmental Modeling, Department of Mathematics, University of Tennessee
- Craig Moritz, Department of Integrative Biology, University of California, Berkeley
- Claudia Neuhauser, Department of Ecology, Evolution, and Behavior, University of Minnesota
- John Pastor, Department of Biology, Center for Water and the Environment, University of Minnesota
- Frede Thingstad, Department of Microbiology, University of Bergen

Beyond emphasizing the spatio-temporal nature of natural systems and the mathematical approaches that are used to address them, this special year was intended to foster interactions between individuals working on problems at different spatial/temporal scales. While the underlying biological questions may operate on quite different scales, the necessary mathematical approaches may be similar. Another theme for the year was linking between scales, for example, how might evolutionary models that account for the dynamics of spatial structure relate to ecological models, which operate on shorter time periods? How might genomic information that is rapidly becoming available assist in developing a theory for whole organism interactions with environment and the functioning of populations, communities, and ecosystems? What new mathematical approaches might contribute to better models for natural system response across the genome/organism/population interfaces? This set of activities enhanced our ability to address these questions and lead to new collaborations between mathematicians and biologists that are beneficial to both fields.

Program Details

Workshop 1: Phylogeography and Phylogenetics
September 26-30, 2005

Organizers: Michael Hickerson (Department of Integrative Biology, University of California, Berkeley), Craig Moritz (Department of Integrative Biology, University of California, Berkeley), and Dennis Pearl (Department of Statistics, The Ohio State University)

Summary of Presentations

The general theme of the workshop was to look closely at the interface between phylogeography and phylogenetics because these two perspectives have a lot to offer each other theoretically and analytically. To this end, sessions on Monday and Tuesday focused primarily on phylogenetic issues, while Thursday and Friday sessions focused on phylogeographic issues, and the middle day concentrated on the interface; this format worked well.

Day 1

The workshop began with a presentation by John Huelsenbeck (UCSD). Dr. Huelsenbeck's work has become crucial to the field of phylogenetics in applying Markov-Chain Monte Carlo (MCMC) techniques to Bayesian tree reconstruction methodology. Importantly, he has lead the effort to develop and deploy MrBayes, a widely used software package to implement these techniques. Besides being involved in general phylogenetic methodology, Huelsenbeck is interested in using DNA variation to detect natural selection, which was the focus of his talk. He told us about a Dirichlet model for accommodating many potential distributions for characterizing natural selection at the DNA sequence level. In the next talk, Elizabeth Allman (University of Southern Maine) talked about a very new approach using algebraic geometry to study phylogenetic invariants. This talk was quite unique and generated much discussion afterwards. For example, she suggested that her approach could help understand the "geometry" of the likelihood function under very general models of evolution and can be used to determine the identifiability of model parameters.

In the afternoon, Mike Steele (University of Canterbury) gave a mathematical tour of the properties of tree shape and metrics, with specific emphasis on how loss in species diversity will affect trees. He started with the classic Yule model, and went through several theoretical results related to phylogenetic diversity. Later in the afternoon, Bret Larget (University of Wisconsin at Madison) led a lively discussion on the various topics raised in the day's talks.

During the evening reception, nine posters were presented on various topics related to both phylogenetics and phylogeography. Each poster highlighted the work of a postdoc or graduate student as author or co-author and, fitting with the intended theme of the workshop, many of the poster presentations were at the important interface between these traditionally different areas. All of the “phylogeographic” presentations were based on gene tree-coalescent models, thereby explicitly taking into account the phylogenetic information in data. Flavia F. Jesus (Universidade Estadual de Campinas, Brazil) presented some impressive analytical results highlighting the general affects that glaciations have on population structure, isolation, and potential for speciation. Liang Liu (OSU) presented work showing how the tree coalescent model from population genetics can be incorporated into a phylogenetic analysis using a Markov chain approach. Craig Moritz and Mike Hickerson both presented posters about comparative phylogeography data (multiple co-occurring species) and the analytical challenges posed by such data. Hickerson’s poster outlined an approximate Bayesian approach that could be quite useful for using such data to detect simultaneous divergence across species. Amy Russell (University of Arizona) presented her phylogeographic analysis of single versus multiple dispersal events for bat species between Africa and Madagascar, while Bryan Carstens (University of Michigan) presented his analysis of the migration of Melanolus grasshoppers, paying particular attention to the effects of sampling issues. Ligia Mateiu (University of Alberta) and Jeff Pan (OSU) each presented generalizations of the standard evolutionary models allowing for variable rates of evolution across sites – Ligia’s work allowing for continuous variation across sites while Jeff’s poster described a model that accounts for the physical distance amongst amino acids determined by the crystallographic structure of a protein.

Day 2

On Tuesday morning, Antonis Rokas (University of Wisconsin at Madison) began the day by showing us a truly “genomic” dataset, and the analytical challenges one faces when using it to make inferences. This talk sparked much discussion throughout the rest of the meeting, and presented a very general important conclusion about Metazoan radiation; that it is hard to resolve its major clades because it happened so quickly. In contrast, Rokas showed this same amount of “phylogenomic” data to be able to resolve major clades of another kingdom of similar age (fungi). However, this study also identified some potential pitfalls and dilemmas when faced with data from many genes, including the bias introduced when treating the data like a concatenated “super-gene.” This theme was touched on in many of the latter talks.

In the late Tuesday morning talk, Marc Suchard (David Geffen School of Medicine, at UCLA) presented a novel approach to a fundamental phylogenetics problem. Almost all phylogenetic analyses are conditioned on a single alignment, rather than incorporating the inherent uncertainty in alignment. Suchard’s solution is to use a Bayesian model for simultaneously estimating the posterior distribution of alignments and the phylogenetic trees that relate the sequences. After lunch, Tandy Warnow (University of Texas at Austin) presented a very different approach to solving optimality problems in phylogenetics. Warnow showed us a “dataset

decomposition technique" arising from graph theory. This strategy appeared to be a promising way to greatly speed up difficult parameter-rich problems in phylogenetics.

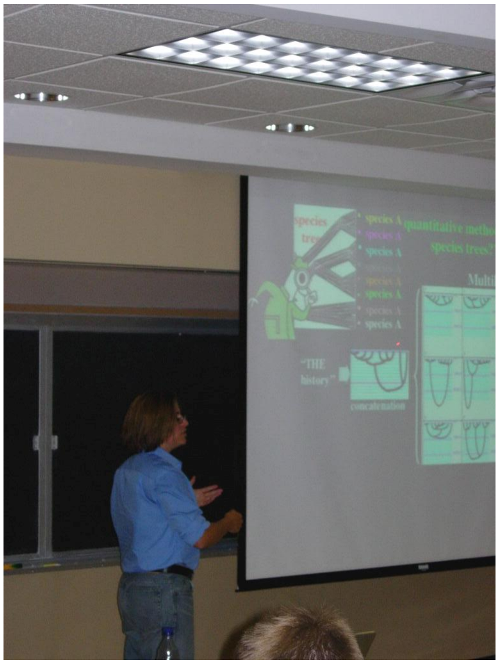
Day 3

As stated above, we intended the third day to be the pinnacle day for the workshop by focusing on the interface between phylogeography and phylogenetics. The day began with Susan Holmes (Stanford University) presenting a phylogenetic decomposition method for detecting selected mutations. Scott Edwards (Harvard University) then gave a broad overview of how shallow-time phylogenetic and phylogeographic studies should proceed in light of theoretical results based on the coalescent, with some examples of very large multi-gene datasets. Edwards highlighted some gaps in the available analytical techniques. In light of real idiosyncratic datasets, he argued that future methods will need to be more flexible and make fewer *a prior* assumptions.

The Wednesday afternoon discussion was one of the highlights of the week, as Noah Rosenberg (University of Southern California) provided a synopsis of one of the most persistent problems in phylogenetics – the importance of incorporating the coalescent into phylogenetic models and the method for treating multi-gene data given that genes may evolve independently with high genealogical variance (e.g., concatenate or majority rule?). By directly incorporating a coalescent model into 4- and 5-taxon tress, Rosenberg presented us with elegant new analytical results showing how the majority-rule method can positively mislead. In fact, his results showed us that under a wide range of conditions, the majority-rule gene tree can converge to the wrong species tree. Rosenberg also referred to related work by James Degnan and Laura Salter (who were in attendance) that provided the analytical underpinning for the conditions under which concatenating multi-gene data will yield wrong species trees. This sparked discussion throughout the meeting involving people from both the empirical and theoretical side of phylogenetics and phylogeography.

Day 4

On Thursday morning, Mark Beaumont (University of Reading) gave a talk on an innovative strategy for analyzing complex parameter-rich phylogeographic data dubbed approximate Bayesian computation (ABC). This approach is approximate in that it does not necessitate calculating the likelihood function when making Bayesian posterior estimates. Instead, one compares summary statistics of the observed data to the same summary statistics calculated over a large number of simulated datasets under a particular model. If there is high correlation between focal parameter values and summary statistic values, then one can accurately estimate these parameters by looking at the subset of simulated parameter values whose corresponding summary statistics are close to the observed summary statistics. An added benefit to this approach is that it is very flexible due to it being based on easy to program simulations, and allows one to ascertain its bias and accuracy without much additional computational cost. Current research will help provide comparisons of the ABC method with more commonly used MCMC methods. This talk provoked much informal discussion throughout the workshop, and even became a formal topic in the Thursday afternoon discussion ("will ABC become the new NCA?" – nested clade analysis). Surprisingly, a number of the participants held strong reservations about ABC and its potential misuse by practitioners.

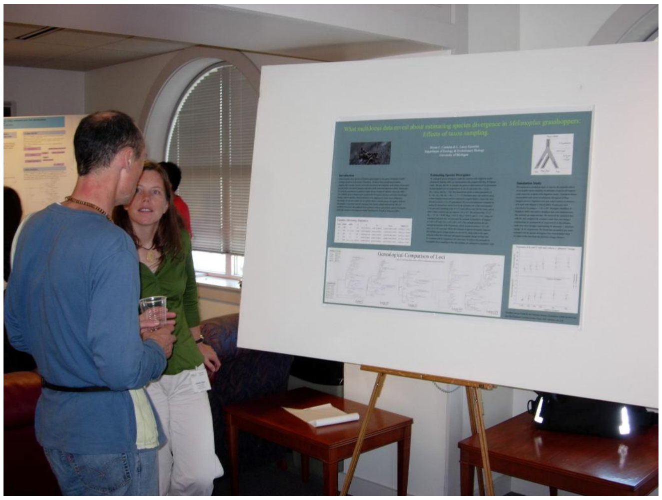


Next, Lacey Knowles (University of Michigan) painted a broad overview of topics and current dilemmas facing phylogeography, and specifically about the workshop's recurrent theme of how the coalescent process can interfere with phylogenetic and phylogeographic inference. Knowles then briefed us on her work that shook up the phylogeographic community a few years ago – a scathing statistical critique of nested clade analysis (NCA). In the afternoon, Stuart Baird (Montpellier) talked about an intrinsically difficult problem for phylogeography – how to spatially incorporate the coalescent onto a continuous landscape. Baird's strategy for this used Wright's classic neighborhood size model implemented on a lattice. Although this allows for Bayesian inference, it also results in some very tricky analytical challenges. In the later afternoon, Peter Beerli (Florida State University) mediated a lively and contentious discussion, touching on an array of issues and problems facing the fields of phylogeography and phylogenetics. This included problems regarding recombination, model-choice and the pros and cons of likelihood, and Bayesian methods. However, this discussion was dominated by the theme concerning the widespread misuse of methods in phylogeography and phylogenetics. Often, particular faulty methodological approaches become "locked in" such that a vast number of empirical studies might be called into question. Although a clear consensus did not emerge from discussion, it was agreed that the peer review system needs to hold higher standards in how a method is deployed, such as demanding that measures bias, error, and model sensitivity of the method be reported to a reasonable degree.

Day 5

Friday morning, took an empirical turn with Chuck Cannon (Texas Tech University) talking about how to use genes to see how tropical tree communities react to large climate change in Indonesia. One of the central dilemmas in this area is that given simple species-area relationships, there are simply too many tree species in light of historical habitat shrinkage. Not only did Cannon show us how he has used integrated phylogeographic and phylogenetic methods to investigate this, he also introduced a potentially profound innovation in how genomic data for such purposes can be collected. This DNA microarray-based technique might provide an effective way to screen many plants at large chunks of their genomes. Following Cannon, Bob Griffiths (University of Oxford) spoke to us about his advanced simulation technique of importance sampling on coalescent histories. Importance sampling appears to work very well under an assumption of non-recurrent point mutations, and will likely provide a fruitful and intuitive strategy for analyzing more realistic data in the future.

Conclusion



The workshop brought together many of the leading experts, as well as talented young scientists, in the field of Phylogeography and Phylogenetics. Overall, the synergistic consequence of having researchers from a variety of areas interact for five days in the invigorating atmosphere of the MBI was immensely successful in fostering collaboration and increased mathematical maturity in these fields. Despite the analytical challenges in obtaining unambiguous answers to complex parameter-rich problems, the workshop revealed a number of hopeful and innovative directions. As demonstrated during the sometimes very vivid discussions during and after the talks, these two fields are undergoing a hybridization. Phylogenetics is starting to incorporate population genetics (the coalescent), and phylogeography is becoming more sophisticated in the way it incorporates the phylogenetic information in data. While this hybridization is essential, it also spotlights the computational and statistical challenges in searching through so large a parameter space. Many participants explicitly commented on how they were stimulated by the relatively loose schedule that allowed plenty of time for interactions among the participants outside of the lectures. Additionally, many of the participants have commented that the workshop continues to be a conduit for collaboration and communication among the disciplines of Mathematics, Applied Mathematics, Statistics, and Biology. It is likely that participants of this workshop will grapple with the challenges brought up with greater clarity and direction for some time.

Workshop 2: Aspects of Self-Organization in Evolution
November 14-18, 2005

Organizers:
Chris Adami and Claus Wilke (Keck Graduate Institute for Applied Life Sciences)

Summary of Presentations

The purpose of this workshop was to bring together different aspects of self-organization in living systems, on as many different scales as possible. Talks were scheduled to discuss self-organization starting from the molecular level (for example in the transition from non-living to living molecular assemblies), in digital, viral and bacterial populations, up to the network level (both from the point of view of molecular interaction networks within a cell and the trophic interaction networks of foodwebs). While the talks were experimental, computational, and mathematical, the emphasis was put on presentations that linked the latest experimental results with mathematical and computational modeling of biological phenomena.

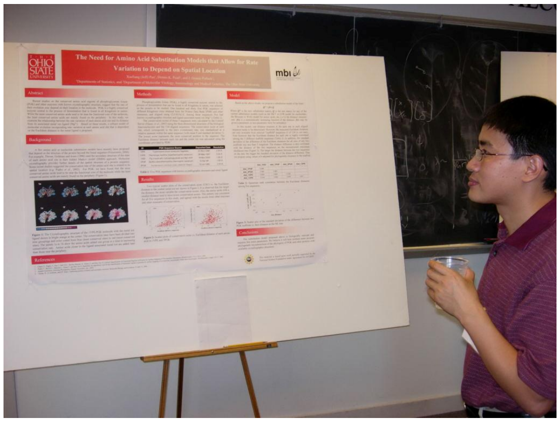
Day 1

The workshop began with a presentation by Liaohai Chen (Argonne National Laboratory) outlining the current efforts to build artificial systems that undergo self-replication of structure and information, that is, artificial living systems. The focus of this work is not to re-create the transition believed to have occurred on the early earth, but rather to understand the principle of self-organization inherent in simple living systems by building *some* system with these attributes, with perhaps very different chemistry from that found in Nature. Chen, in collaboration with Steen Rasmussen, developed a system that consists of replicating vesicles that store the information for their own catalysis in the form of PNA rather than DNA or RNA.

Next, Charles Ofria (Michigan State University) introduced the audience to the concept of "digital life", namely the idea that populations of self-replicating computer programs that have been given the ability to mutate, can live and evolve in computers prepared with the "Avida" software. After a presentation of the main concepts of digital life, Ofria discussed some of the recent research results achieved by using digitals as experimental life forms to study evolution. One particular project he described followed the line of descent of evolution of a complex gene from its final stage all the way backwards to the ancestral simple sequence, mutation by mutation. In this investigation of the evolutionary origin of complex genes, the different mutational mechanisms and interplay between selection and mutation could be observed in detail and show that digital organisms can be an analytic as well as exploratory tool.

The last talk was given by Chris Adami, who discussed the emergence and persistence of genetic diversity in the digital organisms discussed earlier by Ofria. To understand the emergence and stable distribution of species across available niches is still an ongoing problem in evolutionary biology, but progress has been fast in the last five years. For the digital organisms, species diversity was highest if the resources that are used by these organisms for survival are neither overly abundant nor overly scarce. These dynamics can be understood from a simple cost/benefit analysis: it pays to switch to an underused resource only if the common resource is depleted by overconsumption. If the common resource (which is usually the one highest in energy content) is not depleted, switching to a lower energy resource does not pay off. In contrast, switching to a lower energy resource also does not pay off if its renewal rate is small: using this resource will then not pay off for a switcher because there simply isn't enough of the resource present. Theory, in the form of a negative frequency-dependent selection model, predicts the highest speciation rate at intermediate resource abundances. Experimentally (for digital organisms) this prediction is borne out.

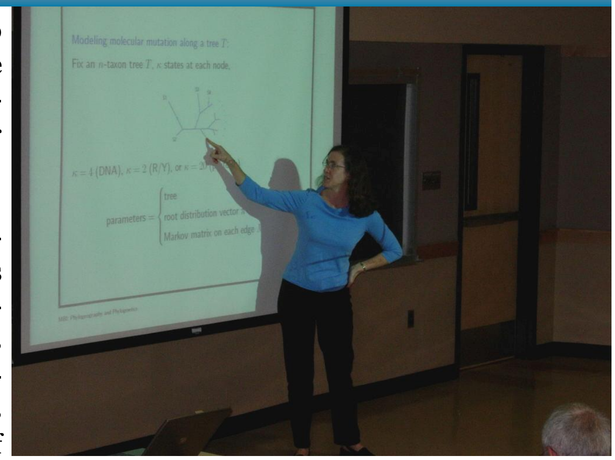
Day 2



Tuesday's focus was on results from viral and bacterial evolution experiments. Around Darwin's time, the only data about evolution that was available were the final results of unintended evolution experiments such as the breeding of cats, dogs, and pigeons (along with the existing natural flora and fauna). Today, dedicated evolution experiments with well-defined boundary conditions can generate data that can be compared with theoretical predictions of the course of evolution. Santiago Elena (IBMCP) presented recent results in viroid evolution. Viroids are plant pathogens that consist of small loops of RNA that are between 300 and 400 nucleotides long. Recent literature in population genetics has identified a new and important component in the fitness of molecules which is mutational robustness. Experiments with digital organisms had previously shown the evolution of mutational robustness at high mutation rates, but this effect had not been seen in biochemical organisms. Elena showed results that suggested that viroids that were evolved at high mutation rates (under the stress of UV lamps) could outcompete faster replicating viroids at high mutation rates but not at low mutation rates, the tell-tale sign of mutational robustness.

Paul Turner (Yale University) next described results from evolution experiments of $\phi 6$ viruses in Pseudomonas bacteria that tested the idea of mutational robustness via the co-infection property of these viruses. The hypothesis implies that selection for robustness would be weakened when the $\phi 6$ viruses evolved at high levels of co-infection, owing to the buffering effect that virus complementation offers. Indeed, this hypothesis was confirmed by the data, via significantly smaller mean fitness of viruses evolved at high levels of co-infection, and a high variance in fitness brought about by the accumulation of random non-lethal mutations.

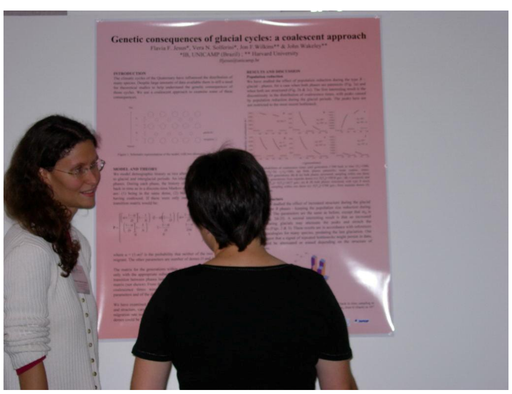
Isabel Novella (Medical University of Ohio) continued the discussion of virus evolution, after first presenting her model system - the vesicular stomatitis virus. Novella discussed the importance of DIPs (defective interfering particles) in virus evolution, via their capability of hitchhiking in healthy virus populations. Experiments with arboviruses (such as the vesicular stomatitis virus), which alternate between arthropod hosts (usually ticks or mosquitoes) and animal hosts show intriguing results that still have no mathematical explanation: the population of viruses appears to split into two subpopulations, which are adapted to either the arthropod or mammalian genes, but are prevented from going to extinction even if their persistence is not selected.



Finally, Eddie Holmes (Pennsylvania State University) discussed other aspects of RNA virus evolution not previously discussed, in particular the origins and evolutionary relationships between different RNA viruses, using bioinformatics methods. He also presented some facts and hypotheses about the rate of evolution of different viruses, in particular the relationship of genetic mutation burden and genome length.

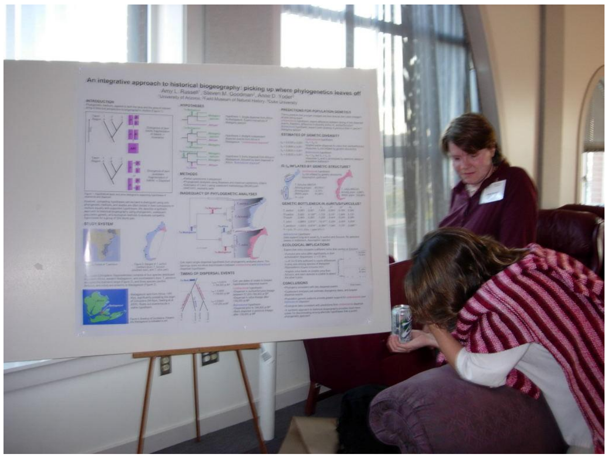
In the evening, a series of posters were displayed, with short talks on selected posters. Emmanuel Tannenbaum (Ben-Gurion University of the Negev) presented the mathematical description of the quasispecies model of evolution for fitness landscapes with multiple peaks for multiple genes. Such a theory shows multiple error threshold transitions, and can be considered a more general (and potentially more realistic) version of Eigen's error threshold. Jan Kim (University of East Anglia) presented a statistical analysis of binding sites in genomes, and a statistical theory that can explain why the ratio of the number of gene binding sites divided by genome length is numerically close to the entropy of binding sites.

Day 3



Michael Doebeli (University of British Columbia) set off the third day with a discussion of the process of adaptive radiation, or adaptive speciation. Recent research has shown that the theory of evolutionary branching may play an important role in explaining speciation events, for both sexual and asexual organisms. Doebeli first gave a brief introduction into this theory. He then presented results from simulations that show that evolutionary branching via negative frequency-dependent selection is very effective in creating segregated populations, but that random mating ultimately destroys the genetic differences. However, a simple model that assumes assortative mating where the mate choice is directly influenced by the segregated trait is effective in maintaining the species separate. Finally, Doebeli presented evolutionary experiments with E. coli bacteria that suggest that ecological diversification via adaptive radiation went on in 9 out of 12 lines evolved to over 1,000 generations.

Michael Travisano (University of Houston) spoke next, first about the mechanics of adaptive radiation, then about the causes for reproductive isolation. While it is known that geographical separation is sufficient to create species by stopping the gene flow between specialized subpopulations, it is not clear whether geographical structure is *necessary* for the emergence and maintenance of genetic diversity. In experiments with Pseudomonas bacteria adapting in a liquid non-stirred medium, experiments showed that spatial structure does not necessarily promote diversity, but rather that the ecological interactions were important. Other experiments with the unicellular (but facultatively sexual) yeast studied the genetic differences responsible for the emergence of species, such as genetic incompatibilities or chromosomal incompatibility. The yeast experiments showed, for example, that tetraploidy rescues gametes otherwise could not mate, showing that chromosomal incompatibility is at the origin of the species difference.



Following Mike Travisano, Arjan de Visser (Wageningen University) discussed the mechanisms of adaptation in small and large populations. In standard theory, the probability for a beneficial mutation, and by extension the rate of evolution of a population, depends on the product of population size and mutation rate. However, subtle effects can muddy this picture. For example, experiments show that in complex environments, the small population has a higher adaptive rate compared to the larger population, while in simple environments, the small population sometimes loses fitness. A possible explanation is that smaller populations take smaller evolutionary steps and thus ascend shallower hills in the fitness landscape, with the possibility that these shallow slopes lead to higher peaks after all.

Daniel Segre (Boston University) ended the day with his work on the origin and evolution of metabolism. He presented results of a simulation of molecular assemblies, where the frequency of each molecule in the assembly is a fixed point, giving rise to genetic "compositional" information. This GARD (Graded Autocatalytic Reaction Domains) model suggests that genetic information could possibly have had a precursor in compositional information. Segre then presented more recent work that studied the effect of perturbations on gene interaction networks whose functions are simulated by a flux balance model that implements mass conservation. In such a model, the effect of single mutations or pairs or multiples of mutations can be investigated computationally by a maximization of the growth rate of the cells using linear programming methods. The interaction between mutations (epistasis) allows a prediction about genetic families or modules within cells that can be tested with known functional or gene ontological criteria. Instead of talks on posters, the evening featured a joint discussion of current topics in evolutionary biology, centering mostly on the concepts of evolvability, adaptability, robustness, and fitness.

Day 4

The day got off to a promising start with Yuri Wolf (NCBI/NLM/NIH) discussing the attempt to uncover unifying measures of gene function and evolution. He asked whether bioinformatics methods could detect which categories are most effective at separating and classifying genes. An extensive analysis of a dataset of clusters of orthologous eukaryotic genes (KOG) identified seven variables that cluster these genes: dispensability, propensity for gene loss, expression level, knockout effect, physical interactions, number of paralogs, gene interactions, and sequence evolutionary rate. A principal component analysis identified two important classifiers that can be identified as “status”, and “adaptability”. Functional classes of genes substantially vary in status and adaptability, with the highest status characteristic of the translation system and cytoskeletal proteins, and highest adaptability seen in metabolic enzymes and transporters.

Claus Wilke then described recent approaches to disentangle the various factors that affect the evolutionary rate of genes in yeast. Using the statistical method of principal component regression, he showed that a single predictor dominates the evolutionary rate of genes, explaining roughly 40% of the variance in both the synonymous and nonsynonymous evolutionary rates; dS and dN. This predictor seems to correspond to the rate of translation of a gene. Interestingly, quantities such as the gene's dispensability (i.e., how unimportant a gene is for yeast) or the number of interaction partners in the protein interaction network play only a minor role in the regression, and have almost no explanatory power for dN and dS. Wilke then presented a hypothesis explaining this observation: selection against protein-misfolding caused by mistranslation in highly-expressed genes is sufficient to generate the observed patterns in dN and dS.

In the afternoon, Dan McShea (Duke University) analyzed the concept of complexity in evolution, and whether it is possible to identify a trend in the evolution of biological complexity. He argued that a measure of complexity that only considers differentiation -a measure he called “pure complexity”- should increase independently of function, and therefore in the absence of selection. Thus, pure complexity should increase spontaneously simply by the accumulation of variation. Selection, instead, attempts to counteract this trend, so much so that pure complexity under selection sometimes drops dramatically.

Tom Schneider (National Cancer Institute) took over to discuss molecular information theory and the evolution of binding sites in bacterial genomes. Schneider argued for a description of molecular information squarely within Shannon’s theory, where probabilities are obtained not by gathering frequencies horizontally (along a gene), but rather vertically, across alignments of the same gene. Such a method can identify binding sites through the pattern of their conservation, and a simple model of binding site evolution in artificial proteins shows the emergence of information in the form of functional binding sites in populations that were informationally inert.

In the last talk of the day, Jim Crutchfield (UC, Davis) studied complexity from a dynamical systems and machine learning point of view. He presented finite state automata that interact to produce new automata: objects that build objects. Such a model allows for an investigation of the emergence of structural complexity across different hierarchical scales. And indeed, the observed tendency was that the structural complexity would increase spontaneously, very reminiscent of the trend in McShea’s pure complexity concept, where selection would then force simplicity to fill out the low complexity niche vacated by the accumulation of structural complexity. It appears that because it is easy to create, by composition, complicated machines in this model, the requirement that they be functional (here, compatible in their input/output alphabet) forces a winnowing down of machines toward the simpler ones. Quite surprisingly, this meeting saw two complexity concepts, one coming from paleontology and one from the mathematics of dynamical systems, merge into one. The evening was capped off by a banquet dinner that saw the last workshop participants retreat to their rooms only in the small hours of the morning.

Day 5

Alpan Raval (Keck Graduate Institute) started out by discussing mathematical methods that could distinguish functional biological networks from random or purely mathematical ones. The most successful such measures examine the position of a gene within a network, and correlate it with the function in a network. For example, essential proteins (those that confer severe disadvantage or death upon the organism when removed) seem to be found more often among the hubs of a gene interaction network, and a positive correlation is found between the number of common nearest neighbors of two genes and the presence of a physical interaction between their proteins. By using measures such as “hub-ness”, “betweeness centrality”, and “clustering” (that can be defined mathematically for each node in its network), functional predictions about the network can be made.

Neo Martinez (Pacific Ecoinformatics & Computational Ecology Lab) gave the last talk, and fittingly his talk addressed self-organization on the highest level, namely the organization of trophic foodwebs. Martinez described an effort to gather data on existing foodwebs, and model their evolution and behavior under perturbations, including their interaction with the environment and primary food resources. Such an effort is geared at understanding which properties of foodwebs are responsible for their stability, and allow dedicated experiments to be performed in simulation that apply directly to the ecology in question.

Conclusion

The workshop was deemed an enormous success by all participants interviewed. The participants came from very different disciplines, and brought together experimentalists, theorists, and computational scientists from biology, mathematics, physics, and computer science. The emphasis in this workshop was not on the presentation of mathematical methods, old or new, that could be useful in solving biological problems, but rather on presenting a tight interaction between experimental and modeling research, and in particular on presenting the latest experimental data that may require new mathematical approaches to describe. The organizers thought that the mathematical audience at the MBI was sophisticated enough that they did not need to be taught theory, but that instead, the direct immersion into the most modern results of evolutionary biology, adaptation, and self-organization would spark new ideas, and possibly the application of familiar methods of mathematics to novel areas in biology. In summary, the workshop provided an extremely stimulating atmosphere in which experimentalists, theorists, and computational scientists all felt they were pulling in the same direction, unified by their interest and passion in understanding the last open questions in adaptation and evolution.

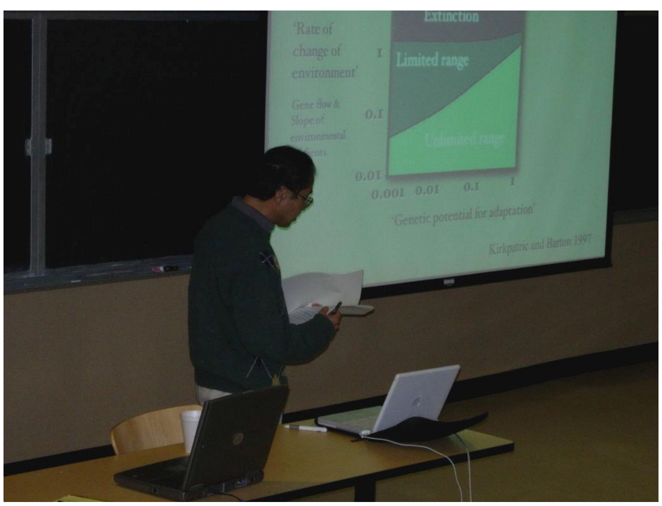
Current Topics Workshop: The Problems of Phylogenetic Analysis of Large Datasets
December 1-2, 2005

Organizers: Daniel Janies (Department of Biomedical Informatics, The Ohio State University), Dennis Pearl (Department of Statistics, The Ohio State University), Diego Pol (Mathematical Biosciences Institute, The Ohio State University), John Wenzel (Department of Entomology, Museum of Biological Diversity), and Ward Wheeler (Division of Invertebrate Zoology, American Museum of Natural History)

Summary of Presentations

Over 65 participants came to the workshop to discuss the problems of large dataset analysis in phylogenetics. These participants were drawn from the fields of systematics, computer science, mathematics, statistics, and biomedicine. This diversity of disciplines reflects the wide applicability of phylogenetics. The participants left the workshop with many new collaborators and a sense that the future of the field was very bright.

Day 1



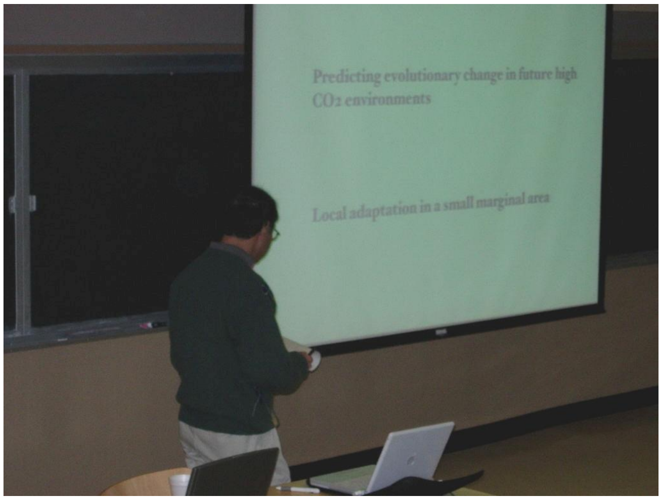
Walter M. Fitch (University of California, Irvine) presented a co-authored paper with Hoang Minh HoDac and Robert Wallace entitled *Inferring migration from phylogenies*. Dr. Fitch first focused on a phylogenetic analysis of 181 hemagglutinin sequences from human viruses of the B type. He then discussed the use of character states for the geographic locations from which the viruses were isolated. Subsequently, he determined a most parsimonious optimization of the geographic vector on the previously determined tree. His aim was that the resulting data would provide insight on the pathways by which influenza viruses spread. Initial results suggested multiple available pathways.

Next, Diego Pol (Mathematical Biosciences Institute) presented a paper co-authored with Pablo Goloboff and Daniel Janies entitled *Strategies for Parallelizing of Heuristic Tree Searches Using Parsimony*. Dr. Pol explored parallel heuristic tree searches for phylogenetic analysis of datasets consisting of 2,000 to 3,000 taxa using the maximum parsimony criterion. The efficiency of alternative strategies was assessed for several benchmark datasets.

The searches were conducted in parallel in Beowulf clusters (using 10 to 60 processors) using several heuristic algorithms implemented in TNT. The identification of an efficient combination of heuristic algorithms and tuning of the algorithms' parameters in the context of the parallel environment was critical to the overall efficiency of the parallel tree search. Stopping rules for the heuristic search were discussed, including the convergence to the best-known score of each dataset during independent trials and the stabilization of the strict consensus of most parsimonious trees. The problems of large datasets with poor phylogenetic structure was discussed through the analysis of 2,359 hemagglutinin genes of influenza type A, which required the use of iterative constraints to achieve independent hits to minimum lengths in reasonable times.

Daniel Janies (The Ohio State University) ended the morning with a talk on *Applications of large-scale phylogenetic analysis for research in emerging infectious disease* (co-authored by Goloboff and Pol). He reported on the application of large-scale phylogenetic analysis to track host shifts and measure surveillance quality among influenza A. Emerging infectious diseases and organisms present critical issues for public health and economic welfare and are thus important to monitor. As demonstrated by the coordinated international response to severe acute respiratory syndrome and avian influenza, emerging infectious diseases are now being addressed via the collection of nucleotide sequence data. However, the ability to derive information from large sequence datasets lags far behind their acquisition. To perform a longitudinal study of influenza A, he used the best data currently in the public domain and performed phylogenetic and character optimization analysis of 2,359 hemagglutinin nucleotide sequences from isolates of influenza A using heuristic searches in parallel TNT. Their phylogenetic analysis revealed multiple independent events of avian to human transmission without intermediate hosts. They also used this large comprehensive analysis to assess the quality of surveillance of influenza A. Compared to a null hypothesis of no correspondence among date of isolation of viruses and the temporal pattern implied by the phylogenetic hierarchy of viruses, their ability to reconstruct the spread of H5 viruses was better than expected.

In the afternoon, Usman Roshan (NJIT-CCS) presented a paper entitled *Co-evolution of DCMs and base-methods for phylogeny reconstruction*. The Disk-Covering Method (DCM) is a divide-and-conquer booster technique for improving upon a given base method. It computes decomposition on the input set of species into smaller overlapping subproblems, applies an external base method to compute subtrees, merges them into a supertree, and further refines the supertree with a local search method if necessary. DCMs have co-evolved with different base methods and optimization criteria since they were first introduced. Dr. Roshan discussed the general framework of DCMs and discussed in detail the dataset decomposition aspect. He presented the successful application of DCMs for large-scale phylogeny reconstruction using: (1) the neighbor joining method (under distance-based reconstruction); (2) GRAPPA (under gene-order data); (3) PAUP* and TNT (under maximum parsimony); (4) RAxML (under maximum likelihood); and (5) POY (under generalized tree alignment). Finally, he highlighted how DCM evolved with the different base-methods and optimization criteria accompanied by various experimental performance studies.



Pablo A. Goloboff (Instituto Superior de Entomología, Consejo Nacional de Investigaciones Científicas y Técnicas) presented *On divide and conquer strategies for parsimony analysis of large data sets*. He discussed rec-i-dcm3, which Roshan et al., 2004 described as a "divide-and-conquer" technique for analysis of large datasets and stated that it compares very favorably to results using TNT (the fastest parsimony program; Goloboff et al., 2003). He argued that Roshan et al.'s claims that rec-i-dcm3 outperforms the techniques in TNT was poorly substantiated. First, the settings they used for the TNT runs were extremely poor; very simple settings for TNT would have done a much better job. Second, having TNT analyze larger sub-problems, with more exhaustive algorithms, produces much better results. In addition, rec-i-dcm3 depends on a global round of TBR after each cycle of subdivision, so that using any program other than TNT as a search engine becomes unfeasible in the case of very large datasets (e.g., for Roshan et al.'s largest dataset, the TBR swapper in PAUP* runs about 800 times slower than the one in TNT). The global TBR becomes more and more critical as the data set is divided into smaller sub-problems because then the combination of the results produces a more suboptimal tree, so that there is a clear limit to the number of taxa that can be reasonably analyzed with rec-i-dcm3. Additionally, since creating reduced datasets to improve the results invariably produced a worse tree, which is subsequently improved by global TBR, rec-i-dcm3 is not truly a divide-and-conquer strategy as publicized, but instead a technique for cyclic perturbations and improvements.

Steve Farris (Swedish Museum of Natural History) ended the first day with a paper entitled *Analyzing Large Data Sets – A Cautionary Tale from Antiquity*. He described that the methods Single-linkage phenetic clustering *seems* an ideal way of finding trees: it can be implemented as an $o(t^2)$ algorithm, and the differences between clustering levels reflect strength of support for clusters. Like all phenetic methods, it can give grotesquely inaccurate trees when the data depart from a clock, but that problem can be overcome by clustering on special similarities $s_{ij} = \frac{1}{2}(s_{ir} + s_{jr} - d_{ij})$ instead of on distances d_{ij} (that formula is now called the Farris transform). In 1992 Dr. Farris wrote a program that used this approach, and it was indeed very fast. However, as he learned soon after, it gave truly pathetic results when the data included many gaps – a failing common to distance methods, although less commonly discussed by their advocates. Thus admonished by experience, he developed parsimony jackknifing instead. This is almost as fast, has no problems with clocks or with gaps, and can indicate group support through resampling frequencies. But why should anyone care about the mistakes of the past? Because in 2002 *the same method* – single linkage on transformed distances – was published *again*, without any mention of earlier work, but this time with simulations to prove that the method is highly effective. The simulations showed this by not including insertions or deletions in the simulation model. So the moral is, those who do not consider earlier work are doomed to repeat its failures.

Day 2

Bernard Moret (University of New Mexico) started the morning with a talk on *Large-scale phylogenetic reconstruction, the Tree of Life, and CIPRES*. He reviewed current computational activities aimed at reconstructing the Tree of Life; the evolutionary history of all living organisms. Researchers and funding agencies worldwide have put renewed emphasis on the establishment of evolutionary relationships among living species because such relationships are fundamental to research in medicine, drug design, agriculture, ecology, and many other areas. The CIPRES (Cyber Infrastructure for Phylogenetic Research) was founded to develop the informatics tools required to attempt a reconstruction of the Tree of Life. Dr. Moret sketched the goal and current achievements of CIPRES, commented on future needs, and related its work to that of other research efforts in phylogeny. He then discussed specific challenges that arise in reconstructing trees with 100,000 or more leaves, with particular emphasis on sources of error and on the methodological advances needed to evaluate the quality of such reconstructions.

Andrés Varón (American Museum of Natural History) presented a paper entitled *Minimum Description Length Phylogenetic Analysis*. With the growing size of molecular datasets, additional transformation events are required under certain, not clearly defined, conditions. Hybridizations, duplications, inversions, tandem repeats, horizontal gene transfers, can be taken into consideration, but their relevance for a particular dataset is difficult to assess. He proposed the Minimum Description Length Principle (MDL) as a more fundamental optimality criterion for phylogenetic inference. Finally, both MP and ML under static and dynamic homologies were shown to be two particular cases of this more general framework.

Ward Wheeler (American Museum of Natural History) discussed *Kolmogorov Complexity, Links with Parsimony and Likelihood, and Tests of Methods and Monophyly*. Kolmogorov Complexity and the MDL Principle provide a foundation to compare and understand the relationship between parsimony and likelihood methods. The case of binary characters was presented showing that condition Kolmogorov Complexity (K) of a cladogram, given the root, is equal to the parsimony score and that the (Tuffley and Steel, 1997) likelihood can be derived from this value via the Universal Distribution. Furthermore, the (Farris, 1973) "maximum evolutionary path" likelihood can be viewed as the composition of edge transformation functions. The role of root complexity was presented in light of tests of monophyly and multiple origins of taxa. An example using metazoan ribosomal data was presented.

The afternoon began with Gonzalo Giribet's (Museum of Comparative Zoology, Department of Organismic & Evolutionary Biology at Harvard University) discussion on *What is large?*

Analyzing sets of unaligned sequence data. He explored the issues of analyzing medium-size data sets when they are not pre-aligned, and the strategies for exploring such datasets. He explained that unaligned data cannot be analyzed efficiently due to the number of possible alignments that exist for a given set of sequences and the number of possible trees for a given number of terminals. Therefore, tree search for unaligned data includes a nested series of NP-hard problems.

Alexandros Stamatakis (Institute of Computer Science of the Foundation for Research and Technology-Hellas) gave a presentation on *Computing Huge Trees with Maximum Likelihood: An HPC Perspective*. The inference of phylogenies based on the Maximum Likelihood (ML) criterion has been demonstrated to be NP-hard. However, over the last couple of years significant algorithmic advances have been achieved that allow for ML-based analysis of 1,000 organisms within less than 24 hours on a single CPU. To date, most state-of-the-art ML programs are limited by their memory consumption to tree sizes of approximately 3,000 to 5,000 taxa. Thus a new category of performance problems arises that mainly concerns technical issues such as memory consumption/organization, cache efficiency, and optimization of the likelihood functions. Using RAxML (Randomized Axelerated ML), Dr. Stamatakis focused on the rarely documented technical implementation details that are of growing importance. RAxML has inherited and extended the extremely efficient implementation of fastDNAml, an unpublished novel, and very simple technical optimization of RAxML, which yields run-time improvements of approximately factor 10 on huge alignments comprising 25,000 taxa. In addition, the exploitation of fine-grained loop-level parallelism on SMPs (Symmetric MultiProcessing) and GPUs (Graphics Processing Units) was addressed. Finally, potential algorithmic and technical challenges as well as solutions for future large-scale inferences of 100,000 taxa were briefly discussed.

Bret Larget (University of Wisconsin, Madison) ended the workshop with a talk on *Bayesian MCMC Approaches for large gene-order phylogenies*. Methods for the analysis of genome arrangements for phylogenetic inference are complicated by the relative size of the space of possible arrangements. Unlike DNA, amino acid, or codon sequences, where sites can be modeled as independent and there are 4, 20, or 61 possible states, genome arrangements must be considered as a single complicated character. In the case of animal mitochondrial genomes with 37 genes arranged on a circle, there are over 2*10^{52} arrangements. This massive state space requires extensive modifications to the algorithms for both likelihood and parsimony based analysis. In this presentation, he described the Bayesian approach to phylogenetic inference from genome arrangements with several example datasets. He also made comparisons between the Bayesian approach and the parsimony approach for genome arrangement data.

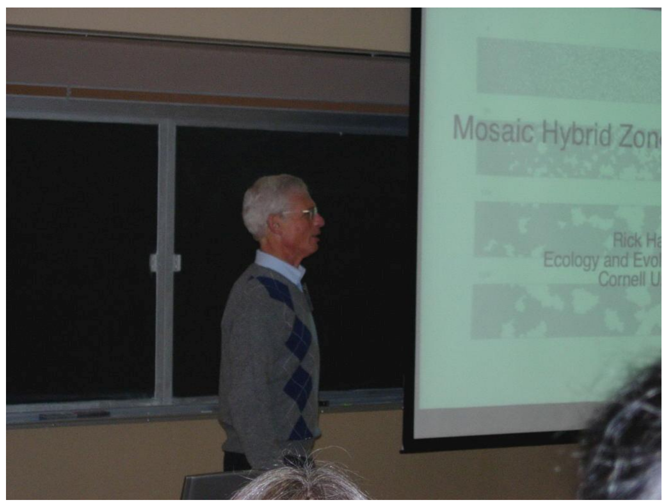
Workshop 3: Spatial Heterogeneity in Biotic and Abiotic Environment Effects on Species Ranges, Co-evolution and Speciation
February 6-10, 2006

Organizers: Sergey Gavrilets (Department of Mathematics, University of Tennessee), Mark Kirkpatrick (Section of Integrative Biology, University of Texas), and John Thompson (Department of Ecology and Evolutionary Biology, University of California)

Summary of Presentations

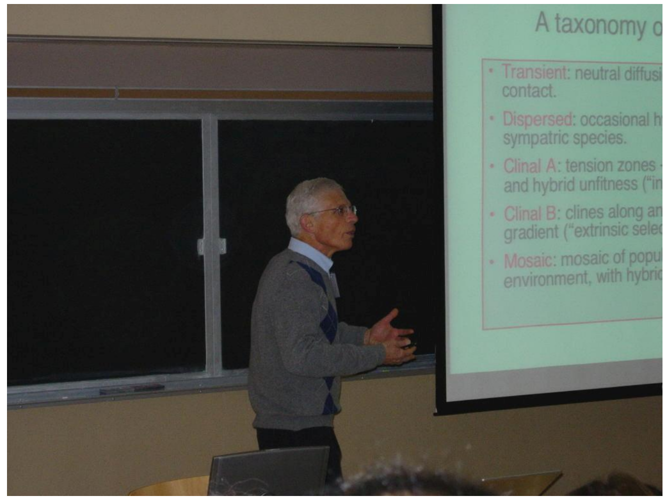
The purpose of this workshop was to bring together physicists, mathematicians, and theoretical and empirical biologists interested in understanding the effects of spatial heterogeneity in biotic and abiotic environments on the properties of evolving populations. In particular, the focus was on the dynamics of species ranges, coevolution, and speciation. The complexity of the evolutionary dynamics driven by ecological and co-evolutionary interactions in a spatially explicit context requires the development of modeling approaches that are both sophisticated and realistic. This is hardly possible without genuinely cross-disciplinary interactions. The workshop was a major step towards establishing such interactions.

Day 1



The workshop started with a talk by Roger Butlin (The University of Sheffield) on adaptation to environmental gradients. Adaptation to environmental gradients has received much attention recently in two contexts: understanding range margins and their response to environmental change, and evolution of reproductive isolation in parapatry. These two issues are linked by common features in the behavior of marginal populations and hybrid zones. The rocky shore snail, Littorina saxatilis, has evolved distinct morphotypes at different points on the steep intertidal environmental gradient. This has apparently happened independently at least three times in Europe. AFLP-based approaches have allowed us to investigate the genetic architecture of these adaptations and the barrier to gene flow that they generate. Roger also discussed some results from an individual-based simulation of adaptation at range margins. This work has focused on the consequences of introducing factors such as mating dispersal and finite population size into the framework developed by Kirkpatrick and Barton. Simulations show that adding these real-world features increases the range of parameter space in which stable range margins occur.

The second talk was given by Ilkka Hanski (University of Helsinki) who focused on spatially realistic models of metapopulation dynamics. Models of metapopulation ecology, genetics, and evolution have tended to assume a simple description of landscape structure, which has hindered the testing of models with empirical data. Recent work has attempted to link a more realistic description of landscape structure with modeling of the ecological metapopulation dynamics. It would be helpful to develop a comparable framework for genetic and evolutionary studies. Ilkka discussed some empirical results on a well-studied butterfly metapopulation, including coupling of the ecological and evolutionary dynamics in host plant selection and evolution of dispersal in fragmented landscapes.



Two talks in the afternoon concentrated on theoretical models of coevolution. Evolutionary biologists have identified several factors that could explain the widespread phenomena of sex and recombination. One hypothesis is that host-parasite interactions favor sex and recombination because they favor the production of rare genotypes. A problem with many of the early models of this so-called Red Queen hypothesis is that three factors are acting together: directional selection, fluctuating epistasis, and drift. It is thus difficult to identify what exactly is selecting for sex in these models. Is one factor more important than the others or is it the synergistic action of these different factors that really matters? Sylvain Gandon (Genetique et Evolution des Maladies Infectieuses) focused on the analysis of a simple model with a single mechanism that might select for sex: fluctuating epistasis. He first analyzed the evolution of recombination when the temporal variation is driven by the abiotic environment. Sylvain then analyzed the evolution of recombination in a specific two-species coevolution model. In this model there is no directional selection (allele frequencies remain fixed), and the temporal variation in epistasis is induced by the coevolution with an antagonist species. In both cases he contrasted situations with weak or strong selection. In the single species model, Sylvain derived an expression for the evolutionarily stable (ES) recombination rate. This ES strategy decreases with the speed of the fluctuations of epistasis, but even when fluctuations are very slow (periods longer than 100 generations) some recombination rates (>0) can be selected for. In the two-species coevolution model, he found that the evolutionary outcome is mainly governed by the maintenance of coevolutionary cycles.

Empirical studies of host-parasite and predator-prey interactions commonly demonstrate local maladaptation in at least one of the component species. These empirical results are in line with theoretical predictions based upon models of host-parasite interactions mediated by simple genetic mechanisms of infection and resistance. The extent to which these theoretical results extend to host-parasite or predator-prey interactions mediated by quantitative traits is, however, unclear. Scott Nuismer (University of Idaho) presented mathematical and numerical results for a model of spatially structured coevolution mediated by quantitative traits. The results demonstrate that local maladaptation is substantially less likely when coevolution is mediated by quantitative traits.

Day 2

The day began with Rick Harrison's (Cornell University) lecture on mosaic hybrid zones. Two papers published in 1986 set forth the notion that some hybrid zones might profitably be viewed as mosaics of populations or genotypes, reflecting an underlying habitat and/or resource template. Rick reviewed the theoretical and empirical literature on mosaic hybrid zones that has accumulated in the past two decades, and discussed the insights that have emerged. He also summarized our current understanding of patterns of variation in a field cricket (Gryllus) hybrid zone that provided the initial motivation for thinking about habitat mosaics and their influence on interactions between hybridizing species.

Next, Masakado Kawata (Tohoku University) discussed speciation by sensory drive through the evolution of visual pigments along an environmental light gradient. Although theoretical studies suggest sympatric and parapatric speciation can occur through disruptive natural or sexual selection, recent re-evaluations of these speciation models indicated that conditions under which this happens are restrictive. Thus, it is important to investigate the probability of such speciation by using models based on explicit genetic mechanisms for female choice and male ornamentation. Masakado first showed that in simulations where the evolution of visual pigments and color perception are explicitly modeled, sensory drive can promote speciation along a short selection gradient within a continuous habitat and population. We assumed that color perception of individuals evolves to adapt to the light environment and that females prefer to mate with males whose nuptial color they perceive most intensively. In his simulations, color perception depends on the absorption spectra of an individual visual pigment. Speciation occurred most frequently when the steepness of the environmental light color gradient was intermediate and dispersal distance of offspring was small. In addition, Masakado's results predict that mutations that cause large shifts in the wavelength of peak absorption promote speciation. The genetic control for male nuptial color also affects the probability of speciation, but far less so then the genetics of female mating preference.

Two talks in the afternoon focused on new mathematical techniques. Species often range over heterogeneous selective environments which, relative to a comparable uniform environment, can have unique impacts on the fate of a new mutation. Different approximations have been developed to characterize the probability of fixation of a new mutation in spatially variable environments for different combinations of migration and selection parameters. However, no single method seems to be accurate for all parameter combinations, and there are some parameter ranges for which no accurate approximation is available. Richard Gomulkiewicz's (Washington State University) talk reviewed the performance of several approximations for the probability of fixation and presented a new approximation, based on separation of the time scales of selection and migration. Simulations he performed with symmetric migration suggest that heterogeneous selection never decreased - and at times substantially increased - the fixation probability of a new mutation compared to a new mutation experiencing homogeneous selection with the same mean intensity. Alan McKane (University of Manchester) discussed a systematic approach to the modeling of biological systems which starts from individual-based models, and then goes on to derive from these the corresponding deterministic equations, which are valid when the size of the system is large. The formalism used to study the stochastic dynamics of the individual-based model is common to a large number of systems, such as models of epidemics, metapopulations, metabolic reactions, biodiversity - including Hubbell's neutral theory - as well as more conventional predator-prey and competition models. In contrast to most previous studies, these processes are modeled using master equations, which allows use to be made of well-established methods from the theory of these equations to analyze their behaviors. The formalism naturally generalizes to spatially explicit models, and I will compare the governing deterministic equations for these systems to those which are normally written down on phenomenological grounds. The consequences of these, and other novel aspects of the master equation description for the systems under consideration, will also be explored. In the late evening Bob Holt (University of Florida) gave a talk synthesizing theory and data on species ranges. In the evening, the participants attended a public lecture by Dr. Ransom A. Myers (Dalhousie University).

Day 3

Edmund D. Brodie (Indiana University) discussed phenotypic mismatches across the geographic range of a predator-prey arms race. Coevolutionary interactions between species take place over a wide geographic scale. Population subdivision across that range and spatially variable selection within it may lead to a mix of local adaptation and maladaptation for a pair of interacting species. Toxic newts of the genus Taricha and their resistant garter snake predators in the genus Thamnophis illustrate this general pattern throughout their concurrent ranges in western North America. Understanding of the mechanisms of toxicity and resistance in this system allows us to evaluate the degree of ecologically relevant phenotype matching at any given locality. The resultant picture suggests that nearly half of localities are so phenotypically mismatched as to prevent direct reciprocal selection at present. In at least some of these populations, snake predators seem to have 'won' the arms race by evolving sufficiently high levels of resistance to withstand the effects of any observed level of toxicity. The genetic basis of resistance in garter snakes is at least partly understood and Edmund's results suggest that these mismatches may result from single amino acid substitutions in the sodium channels of resistant snake populations. Craig Benkman (University of Wyoming) talked about a coevolutionary arms race causing ecological speciation in red crossbills. He showed that divergent selection as the result of a coevolutionary arms race between red crossbills (Loxia curvirostra complex) and Rocky Mountain lodgepole pine (Pinus contorta latifolia) in the South Hills promotes

ecological speciation in crossbills. Less than one percent of 1,285 breeding South Hills crossbills paired with non-South Hills crossbills indicate considerable reproductive isolation. The low frequency of heterotypic pairing was the result of at least three factors. One was related to enhanced seed defenses of lodgepole pine in the South Hills and adaptation of each call type to alternative resources with South Hills crossbills depressing seed availability so that few of the other less well adapted call types persisted in the South Hills (competitive exclusion causing habitat isolation). Another pertained to temporal isolation. When crossbills of other call types moved into the South Hills late in the breeding season, feeding conditions were deteriorating because of seed depletion by crossbills (another competitive effect) so that relatively few non-South Hills crossbills bred. Finally, among those crossbills that bred, pairing was strongly assortative by call type (behavioral isolation) further contributing to reproductive isolation between South Hills crossbills and the two other call types most common in the South Hills (call types 2 and 5), with total reproductive isolation summing to 0.999 on a scale of zero to one.

In the afternoon, Sergey Gavrilets described a large-scale, stochastic, spatially explicit, individual-based model of adaptive radiation driven by adaptation to multidimensional ecological niches. His results provide theoretical support and explanation for a number of empirical patterns including "area effect", "overshooting effect", "least action effect", as well as for the idea of a "porous genome." His findings suggest that the genetic architecture of traits involved in the most spectacular radiations might be rather simple, and that a great majority of speciation events are concentrated early in the phylogeny. John Thompson talked about geographic mosaic theory of coevolution. Long-term coevolution of species is an inherently geographic process. It is shaped by geographic selection mosaics that create spatially structured coadaptation among pairs and groups of species. It is further fueled by gene flow and by coevolutionary coldspots where one species falls outside the geographic range of the other species or by lack of reciprocal selection in some coexisting populations. In addition, the coevolutionary process is continually reshaped by the appearance of new tips on phylogenetic branches as some locally coevolving populations diverge into coevolving sibling species complexes. These dynamics of coadaptation and speciation are the interface of microevolution and macroevolution in coevolutionary biology.

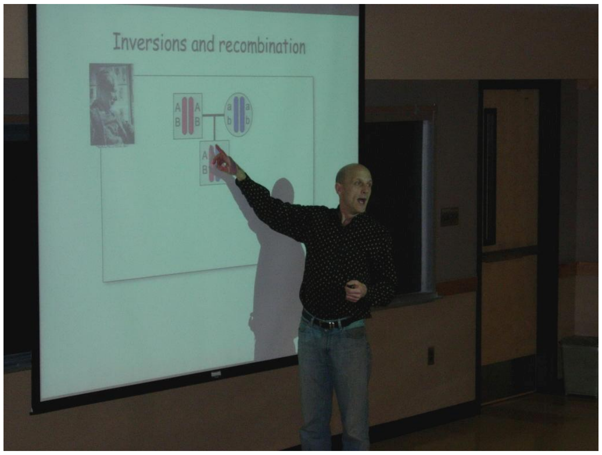
Day 4

Jane Hill (University of York) discussed evolutionary changes during climate-driven range expansion. Some species are responding to current global climate warming and shifting their distributions polewards and/or uphill. It is becoming clear that evolutionary changes are occurring as a consequence of this climate-driven range expansion. Evidence for increased dispersal ability, shifts onto novel host-plants and increased ability to tolerate poor larval host-plant quality in populations at expanding range margins suggest that some species may be able to keep track of environmental changes. However these changes are balanced by evolutionary trade-offs in fecundity, and most species are failing to expand due to loss of breeding habitat, regardless of any evolutionary adaptations. In addition, reduced genetic diversity in populations expanding through patchy habitats is also likely to affect species' ability to respond to novel environments. Laurent Excoffier (University of Bern) described the consequences of different types of range expansions on several aspects of neutral molecular diversity within and between populations. These results have been mainly obtained by simulations. He first reported on the consequences of a spatial expansion in an empty and homogeneous environment modeled as a 2D stepping-stone, showing that the pattern of genetic diversity within demes mainly depends on the age of the expansion, as well as on the amount of migrants exchanged between neighboring demes. Analytical results obtained under an infinite-island model support these conclusions. Laurent also introduced a model of spatial expansion into an occupied environment, with explicit modeling of interpopulation competition. An interesting prediction of this model is that invading populations should have their gene pool invaded by the resident population if interbreeding is possible between the two competing populations.

In the afternoon, Troy Day (Queen's University) focused on evolutionary change in spatially distributed populations from a kin selection perspective. Historically, a great deal of research in theoretical evolutionary ecology has modeled biological populations by supposing that the population size can take on any of a continuum of values. This assumption is reasonable so long as the population size is relatively large. Much of this research has ignored the consequences of the spatial distribution of populations, but the last couple of decades have seen an increased interest in developing explicitly spatial models for ecological and evolutionary processes. Interestingly, many of these models continue to assume that population sizes at each spatial location can take on a continuum of values. This assumption is often questionable because, although many real biological populations are relatively large, they are often distributed across a spatial range; such local population sizes are quite small. Troy discussed these issues in more detail, and presented some theoretical results illustrating how such finite local population sizes can influence evolutionary change.

Henrik Jensen (Imperial College London) reviewed the attempt within the Tangled Nature model to understand the effect of evolution and interaction on ecological and evolutionary observables. He reported on the relation between the interaction structure in genotype space and the resulting Species Abundance Distribution. Ecological relevant SADs are only obtained if the genotype space allows for a potential high connectivity between species. Henrik also studied the relation between the degree of genotype interaction and species diversity. Furthermore, he included spatial degrees of freedom to investigate the Species Area Relation from an evolutionary perspective.

Day 5



On the last day of the workshop, Mark Kirkpatrick outlined a series of novel theoretical results on the implications of chromosome inversions for local adaptation and speciation. Specifically, he looked at models for the evolution of inversions that capture locally-adapted alleles when two populations are exchanging migrants or hybridizing. By suppressing recombination between the loci, a new inversion can spread. Neither drift nor coadaptation between the alleles (epistasis) is needed, so this local adaptation mechanism may apply to a broader range of genetic and demographic situations than alternative hypotheses that have been widely discussed. The mechanism can explain many features observed in inversion systems. The mechanism can establish postzygotic barriers and thus contribute to speciation: it can establish underdominant inversions that decrease heterokaryotype fitness by several percent if the cause of fitness loss is structural, while if the cause is genic there is no limit to the strength of underdominance that can result. The mechanism is expected to cause loci responsible for adaptive species-specific differences to map to inversions, as seen in recent QTL studies. In the final talk of the workshop, Jim Mallet (University College London) discussed sympatric speciation concentrating on cases of Lepidoptera speciation. Jim argued that many cases of intermediate speciation occur in sympatry, both just below the traditional species level, and just above. The coexistence of these intermediate stages in nature suggests that the whole process of speciation isn't as difficult as all that, especially given local spatial variation in ecological factors. Whether you call this "sympatry" is a matter of taste, but Jim was arguing that it is sensible to do so, at least if one wants any natural populations to be classified as "sympatric" at all. According to Jim, the idea that speciation in the presence of gene flow is difficult seems merely to be an artifact of a rigid and highly non-Darwinian idea: that species are "real" (whatever that means). They are also regarded as "the only real taxon". This was proposed along with the "biological species concept" around 65 years ago, coupled with lots of naiveté about the supposed power of gene flow. Natural populations are telling us that "species reality" and the concomitant "difficulty of speciation" are both greatly overstated. Instead, species are demonstrably continuous with "varieties" in nature, and the evidence of continuous speciation processes is all around us. Jim believes it would solve a lot of problems to go back to a much more pragmatic view of species and speciation, closer to Darwin's own ideas.

Conclusion

The schedule left plenty of time between the talks and in the evening for informal interactions, and all participants took advantage of this. Overall, the workshop was viewed as a great success by all participants. A number of them explicitly stated that both the formal talks and informal interactions have been extremely stimulating, and in a number of cases identified new directions for their research. This is true with regard to both empirical biologists and theoreticians. The general feeling was that bringing mathematical methods and models into the studies of species ranges, coevolution, and speciation has already significantly extended our understanding of these biological phenomena and that more exciting insights were coming soon. Mathematicians and physicists were very pleased to find new, biologically inspired, mathematical problems to tackle. Everybody was also very happy with the organizers and facilities. Many people expressed interest in attending other similar cross-disciplinary workshops at the MBI.

Workshop 4: Spatial Ecology
March 13-17, 2006

Organizers: Chris Cosner (Department of Mathematics, University of Miami), Lou Gross (Departments of Ecology & Evolutionary Biology, & Mathematics, University of Tennessee, Knoxville), Mark Kot (Department of Applied Mathematics, University of Washington), and Claudia Neuhauser (Department of Ecology, Evolution, and Behavior, University of Minnesota)

Summary of Presentations

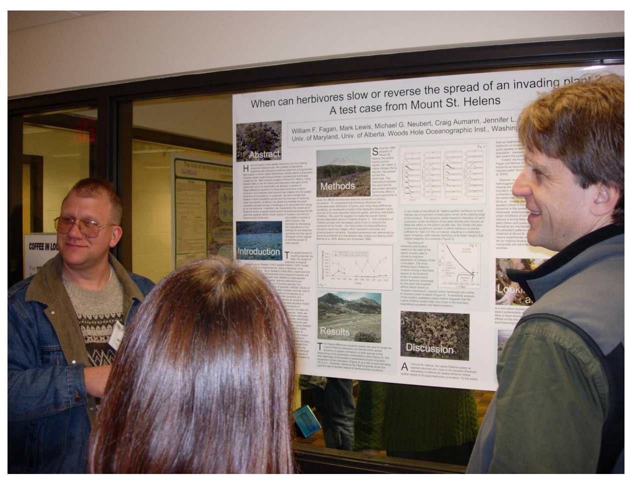
The workshop began with an introduction by Louis Gross placing the workshop in the context of the special year on Ecology and Evolution and noting that an objective of the organizers of the special year was to emphasize spatial issues at several scales. Gross noted that the challenges in spatial ecology might be considered as those associated with: linking across scales; linking to data; and linking across disciplines. Issues associated with each of these were presented and were used as an initial set of questions to be addressed in the workshop breakout sessions. A summary report of the four breakout sessions, focused on issues at population, community, and landscape scales, as well as one focused on the connection between theory in ecology and economics, is being prepared as a separate report. As part of the introductory portion of the Workshop, Chris Cosner (University of Miami) provided a rapid, concise summary of the major foundations of reaction-diffusion equations as applied to ecological systems, as a summary of the pre-workshop tutorial session he led on this topic.

The workshop included a series of formal presentations and associated discussion sessions, as well as a poster session, brief five-minute quick presentations by younger researchers in attendance, and the breakout sessions. The formal presentations ranged in content from those with more of an emphasis on biological data to those with newly developed mathematics. The first presentation was by Sandy Liebhold (USDA Forest Service) who discussed data and modeling issues associated with forest insect outbreaks. Datasets on such populations have long presented a variety of challenges to population biologists and Sandy pointed out how recently available spatial data have led to new efforts to characterize the spatio-temporal projection of outbreaks. While the most striking temporal pattern evident in these data is the existence of periodicity in the presence of regional outbreaks, the most striking characteristic of the spatial dynamics of virtually all species investigated is spatial synchrony (coincident changes in abundance among geographically disjunct populations). The ubiquitous presence of spatial synchrony provides an enticing challenge for population ecologists because this behavior may be caused by several different types of processes, most notably by a small amount of dispersal among populations or by the impact of a small but synchronous random effect, such as variation in weather. By comparing patterns of spatial synchrony among various species with varying dispersal capabilities, Sandy and his collaborators concluded that regional stochastic effects are the most likely cause of the ubiquitous synchrony in dynamics.

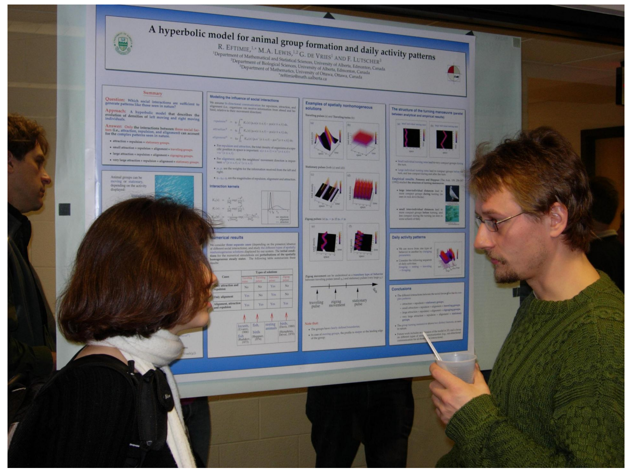
Continuing on the theme of stochastic effects in spatial systems, Otso Ovaskainen (University of Helsinki) presented a new method for the analysis of continuous-space, continuous-time stochastic, and spatial systems that are based on a systematic perturbation expansion of the underlying stochastic differential equations. The method allows one to analyze the spatial and stochastic model in an asymptotically (as interaction range tends to infinity) exact manner. Comparison with simulations shows that the results are not only symptotically correct but often as well as when interactions are due to a few interacting neighbors. Applications of this method were discussed concerning (i) metapopulation dynamics in a correlated and dynamic landscape, (ii) the effects of habitat loss and fragmentation, and (iii) the effects of space and stochasticity on a community of competing plant species. Utilizing an alternative methodological approach to consideration of stochastic spatial analysis, Claudia Neuhauser (University of Minnesota) considered spatial models for the effect of symbiotic interactions on plant community structure. Claudia introduced a spatially explicit, stochastic model based on interacting particle systems that confirms the effect of habitat coarseness on specialization in the absence of coevolutionary processes. To understand the effects of coevolutionary processes, she introduced feedbacks between hosts and their symbionts, finding that mutualists modify their habitat so that it becomes coarse-grained, and parasites modify their habitat so that it becomes fine-grained, suggesting that

the lifestyle of the symbiont prevents habitat types from becoming extreme.

An objective of this workshop was to focus discussion on spatial aspects of optimal control theory as it applied to a variety of important questions in applied ecology. Michael Bevers (USDA Forest Service) provided an overview of the mathematical programming approaches he has devoted two books to, with particular emphasis on optimal risk management of natural resources. He utilized chance constraints in a spatial mathematical programming context to integrate risks associated with uncertainty into plans for optimal management. He presented a numerical estimation method in application to a habitat restoration problem. Suzanne Lenhart (University of Tennessee) presented initial results of efforts to develop a theory of optimal control for spatial problems associated with integrodifference equation population models. These equations are discrete in time and continuous in space. Optimal control of such hybrid systems is a new area and involves a combination of the techniques from the discrete version of Pontryagin's Maximum Principle and from control of partial differential equations. She presented some analysis, characterizations of optimal controls and numerical illustrations for several population models. Louis Gross discussed control problems at regional scales including the addition of control to relatively simple invasive plant species models accounting for a central focus and outlier populations. The expansion of this to a more realistic model for spatial control of invasive plants with application Lygodium macrophyllum in south Florida was presented as well as how spatial aspects of preserve were linked to an individual-based model of black bears in the southern Appalachians. Expanding the control perspective to incorporate economic concerns, Mike Neubert of the Woods Hole Oceanographic Institution discussed spatial aspects of fisheries models to determine impacts of economics on maximum sustainable yield in the face of regulations. While taking account of the open-access nature of most marine fisheries, he presented results on the maximum sustainable economic rent that can be obtained using various policy instruments (including taxes on aggregate effort, taxes on aggregate catch, effort quotas, and catch quotas). The solutions were contrasted with that of a rent-maximizing distribution of effort employed by a sole owner and to the distribution of effort in the unregulated open access case. In many cases, the solution contains unexploited regions in space.

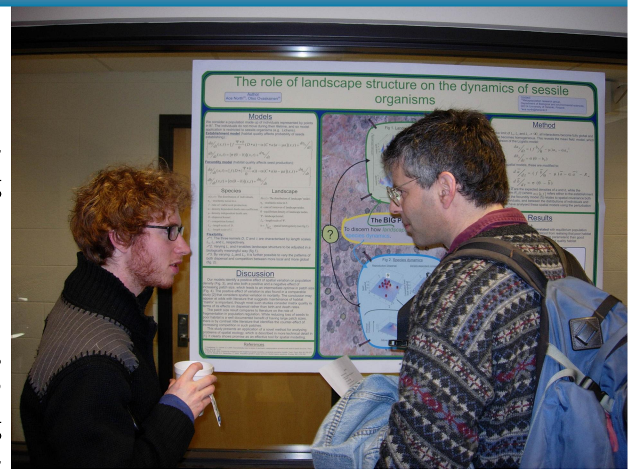


A major thrust of mathematical models in spatial ecology has been to project the behavior of species invading a new region and several presentations focused on aspects of this. Nanako Shigesada (Doshisha University in Japan) has been a long-term investigator of mathematical models for invasives, and she presented recent work on the impact of habitat fragmentation on the spread of an invasive species. She considered invasions in landscapes generated by segmenting an original favorable habitat into regularly striped, island-like, corridor-like, or randomly patched pattern by modifying the Fisher reaction-diffusion equation to include spatial growth rate and diffusion coefficient. Range expansion of the invasive was determined by examining the traveling periodic wave speed in the various environments. This allowed determination of how the pattern and speed of the range expansion are affected by the size of fragmentation, and the qualities of favorable and unfavorable habitats. Mark Kot (University of Washington) elaborated on his efforts to analyze invasive spread through the use of integrodifference equations which he pioneered in applications to population modeling. He presented new efforts to link deterministic integrodifference equations to stochastic branching random walks, and illustrated how these models shed light on the spread rate of invading organisms.



The impacts of spatial heterogeneity in natural systems can be investigated using numerous methods. Daniel Grunbaum (University of Washington) presented methods to determine appropriate functional response curves, utilized in most population dynamic models to determine growth rates of a trophic component as a function of resource density, for spatially and temporally heterogeneous ecological systems. In most ecological systems, resources and consumers are very heterogeneous in time and space, implying that a given quantity of resource can be distributed in many ways, some of which result in higher consumption rates than others by specific types of consumers. He illustrated from this that functional responses cannot be functions only of mean resource and consumer densities, but involve other parameters, which he showed how to determine, and how they might be used to derive differential equation approximations for mobile consumers of heterogeneous resources. Frithjof Lutscher (University of Ottawa) focused his remarks on models for riverine systems, pointing out the unique mathematical challenges associated with ecological systems in these contexts. He particularly focused on the “drift paradox”: how populations in rivers can persist despite flow-induced washout. Starting from a reaction-advection-diffusion equation used to explore persistence criteria by looking at the minimal domain, he reported on several extensions, namely vertical structure in the population, spatial heterogeneity and the influence on channel geometry, effects of resource gradients, and competition of two species.

Breakout Session Summary and Workshop Conclusions

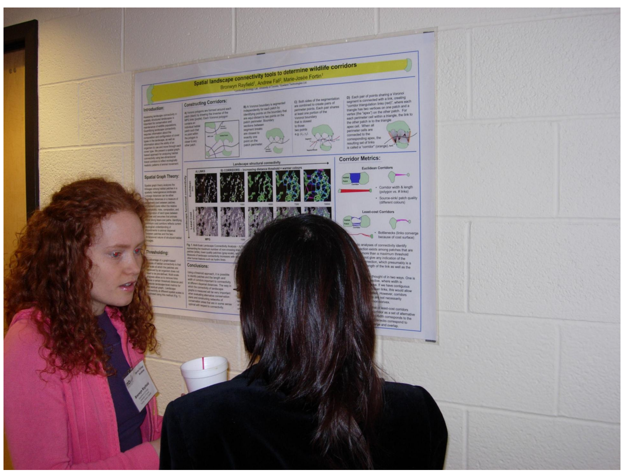


The four breakout sessions focused at different levels of organization on the following questions:

Linking across scales

- How do we most effectively link models operating at different spatial resolutions? Beyond slow-fast time scale decoupling and broad vs. fine spatial extent, (or metered models) what other approaches are useful?

- What can we utilize from other areas of applied math that have developed hybrid modeling approaches?



- How do we compare and contrast different approaches to link models between scales and tease apart how different results arise from the model components at each scale?

Linking to data

- How do we use the plethora of newly arising data from observatories, LTER sites, sensors, and satellite imagery in model selection and evaluation? For example, how do we best use these data to enhance and evaluate the plethora of approaches to invasion biology?

- How do we determine which patterns are the most appropriate to use when comparing models to data?

- How do we train our students (and ourselves) in spatial statistics in order to most effectively utilize the data available and enhance the use of models to guide monitoring programs?

Linking across disciplines

- How can we more effectively utilize advances at genome and individual-level (physiology and behavior) to improve our models at other organizational levels, and how can our models inform those working at these individual levels as to the importance (or lack thereof) of their efforts?

- How can spatial ecological models better inform evolutionary questions including the evolution of dispersal, and the processes that give rise to range limits?

- How can we effectively link spatial processes to human systems issues, accounting for economics, human cultural differences, and the need for resource management? How can we best recommend spatial approaches to be used in setting public policy?

- How do we encourage collaborative efforts and educate our students across the broad array of topics needed to be effective collaborators?

These questions engendered a great deal of discussion at the breakout sessions which were led by Ben Bolker (University of Florida), Linda Allen (Texas Tech University), Will Wilson (Duke University), and Guillermo Herrera (Bowdoin College). Each session involved three meetings of 8-15 individuals from those participating in the workshop, and each group presented a summary of their deliberations to the entire workshop for additional comments. A very lively discussion ensued.

Conclusion

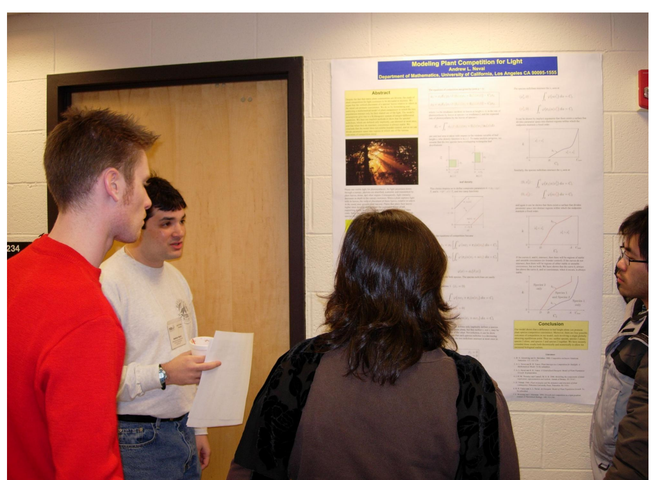
The workshop brought together a highly interactive mixture of established and younger researchers from several countries who have been leaders in spatial ecology, including theoreticians, mathematicians, economists, natural resource managers, and field biologists. The breakout sessions provided opportunities for broad discussion on topics that were elaborated upon in the formal presentations as well as some that were new to the MBI, including issues of bioeconomics. While including some areas of research, which have been extensively investigated with mathematical approaches, the workshop also focused on several newer areas in which the mathematical analyses are quite fresh and require new insights. As a concluding session, the organizers led a discussion of educational issues, noting the vast opportunities arising from new publicly available geographic information systems, associated spatially-distributed sensors for various biological and physical aspects of natural systems, and the potential for these to enhance the spatial comprehension of our students and colleagues.

Second Young Researchers Workshop in Mathematical Biology March 27-30, 2006

Organizers: MBI Postdoctoral Fellows

Overall Summary

The aim of this workshop was to provide a forum for approximately 60 young mathematical biologists to interact with their peers, to broaden their scientific perspective, and to develop connections that will be important for their future careers. It was the second occurrence of what has become an annual event due to the success of the First Young Researchers Workshop, held at the MBI during spring 2005.



The workshop participants (postdoctoral researchers, tenure-track faculty, and advanced graduate students) represented diverse areas of mathematical biology, so participants were able to see some of the breadth of research activity at other universities and institutes. The schedule was structured to encourage interaction among participants, especially to foster free discussions and the initiation of collaborations.

The workshop also featured the participation of eight leading researchers in the mathematical biosciences. They gave plenary presentations and interacted with the young participants. All young participants had an opportunity to present their work by bringing a poster, which they introduced by giving a brief talk during a morning session and later presented during an afternoon poster session. Each poster was displayed for a full day, allowing additional time for discussions during lunch and coffee breaks.

For two of the days, MBI postdoctoral researchers suggested topics for working group discussions and facilitated these discussions at the end of the morning session. Lunch was catered on these days to allow discussions to continue through the lunch break. Each working group summarized their discussion for all participants during the afternoon session, amid further discussion. These working groups addressed broad scientific and career issues such as the history and future of mathematical biology, its coherence as a scientific discipline, job opportunities, and establishing good collaborations. On days without working group discussions, MBI postdoctoral researchers led groups of participants to local restaurants. Interactions among participants were lively and ongoing during the various social events as well as during poster and discussion sessions.

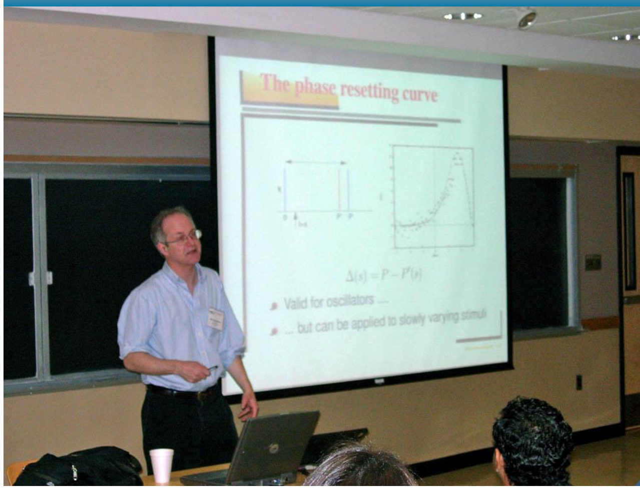
Summary of Presentations

Day 1

Arthur Sherman (N.I.H.-N.I.D.D.K.-M.R.B.) opened the workshop, presenting a model for metabolic and electrical oscillations in insulin-secreting pancreatic beta-cells. The model adds oscillations of glycolysis to earlier models that were based on ionic mechanisms such as calcium negative feedback onto potassium channels and sodium pumps. The metabolic oscillations account for experimentally-observed oscillations occurring on slower time scales than can be accounted for in the previous models.

Short talks by some of the young participants filled out the first morning (for a list of speakers see [1] below). The purpose of this session was to preview the posters that were on display throughout the day and that were also presented during the afternoon poster session. These brief talks also served to introduce the speakers, helping participants get acquainted. The talks covered such diverse topics as using differential geometry to study transmembrane protein structure and cellular automata models of pollen dispersal.

In the afternoon, Catherine Carr (University of Maryland) discussed the evolution of sound localization circuits, addressing a controversy



concerning the nature of the neural code for interaural time differences. She explained a recent proposal that animals should have either a map-like place code or a rate-based population code, according to an optimal coding strategy that depends on head size and sound frequency. By showing that, contrary to the predictions of optimal coding theory, common ancestry rather than physical prerequisites predict the code inferred from data in the chicken, she re-opened the question of what determines neural coding strategies.

Day 2

The second morning began with Bard Ermentrout (University of Pittsburgh) discussing what one can learn about neuronal firing patterns by regarding neurons as nonlinear oscillators. He introduced the spike-triggered averages and poststimulus time histograms that experimentalists commonly use in studying neuronal responses to stimuli. He then showed that under certain circumstances there is a 1:1 mapping between these and a third approach -the phase resetting curve- which has been shown to be tightly coupled to neuronal dynamics. This relation connects the internal dynamics of neurons with their preferred stimuli and their population responses.

A second round of short talks by young participants completed the morning program (for a list of speakers see [2] below). Probabilistic models of neural timing in the mammalian auditory system and an immersed boundary method approach to the study of tiny insect flight were among the topics represented in this set of short talks. The corresponding posters were displayed throughout the day and presented by the speakers during an afternoon poster session.

Leah Edelstein-Keshet (University of British Columbia) spoke in the afternoon, describing recent work modeling the role of the bipolymer actin in cell motility. She showed how the branching of actin filaments and the forces they exert on the cell membrane account for the protrusion velocity and characteristic actin density profiles. She also showed how the interplay between signaling proteins and the actin cytoskeleton accounts for the ability of the cell to maintain a stable shape and speed and to respond to new external signals.

The afternoon also featured Timothy Secomb's (University of Arizona) discussion of mathematical modeling of the microcirculation, which is an extensive branching network of microscopic blood vessels where oxygen exchange with tissue occurs by diffusion. He presented models for the mechanics of blood flow in capillaries, for oxygen exchange between blood and tissues, and for structural adaptation of blood vessels. He discussed the regulation of blood flow over short and long time scales and applications to disease states.

Day 3

Philip Maini (Oxford University) opened the third day of the workshop with a presentation on modeling cancerous tumor dynamics. He addressed different ways of modeling tumor growth and a multiscale model for tumor growth. This lecture was followed by a third group of short talks by 13 young researchers (for a list of speakers see [3] below), advertising their research interests and their posters. Topics ranged from the effects of control stages of new emerging diseases to an integrative computational model of multiciliary beating.

The morning session continued with working group discussions over lunch. The topics chosen by MBI postdoctoral researchers were: (1) *History and Future of Mathematical Biology: Part I*; (2) *Graduate and Undergraduate Training in Mathematical Biology*; (3) *Establishing Good Collaborations*; and (4) *Job Opportunities for Young Researchers in Mathematical Biology*. All the participants chose one of four topics and separated into four groups.

In the afternoon, the representatives from each group reported the summary of their discussions to all workshop participants and further questions and opinions were actively expressed and debated. This afternoon session ended with the poster session by the morning presenters.

Day 4

The first session started with two plenary talks, Kristin Swanson (University of Washington) followed by Hans Othmer (University of Minnesota). Kristin presented applications of quantitative modeling in the clinical imaging of invasive brain tumors. She demonstrated how quantitative modeling cannot only shed light on the spatio-temporal growth of gliomas but also can have specific clinical application in real patients. Hans talked about deterministic and stochastic models of actin dynamics, specifically on the evolution of the distribution of filament lengths and nucleotide profiles of actin filaments.

The second working group session proceeded in the same way as the first, dealing with four different topics: (1) *History and Future of Mathematical Biology: Part II*; (2) *Interdisciplinary Research and What Kind of Training it Requires*; (3) *Principles of Modeling in Mathematical Biology;* and (4) *Will Mathematical Biologists Change the Way Mathematics Departments are Funded?* A summary report from each group followed, and there were questions and comments on each topic.

Conclusion

This workshop followed the overwhelmingly successful First Young Researchers Workshop. Throughout the workshop, the plenary speakers had an opportunity to meet young researchers in mathematical biology and provided challenges and advice. The young researchers with different backgrounds in mathematical biology had chances to meet future colleagues and broaden their knowledge and understanding from plenary talks and poster presentations. The feedback from all participants was very positive and encouraged organizers to continue the Third Young Researchers Workshop.

References

[1] Srisairam Achuthan, Jung-Ha An, Erik Andries, Tanya Baker, Khalid Boushaba, Chad Brassil, David Chan, Gheorghe Craciun, Elena Dimitrova, Jonathan Drover, Nicholas Eriksson, Chris Fall, Jonathan Forde, Boyce Griffith.

[2] William Heuett, Monica Hurdal, Jozsi Jalics, Jerome Jourquin, Abdoul Kane, Trine Krogh-Madsen, Alexey Kuznetsov, Anna Kuznetsova, Joyce Macabea, Ana Margarida Martins, Lorin Milescu, Laura Miller, Maya Mincheva, Colleen Mitchell.

[3] Anuj Mubayi, Baochi Nguyen, Hoan Nguyen, Remus Osan, Michael Raghib Moreno, Karen Rios-Soto, Leonid Rubchinsky, Gabriele Sirito, Peter Thomas, Yulia Timofeeva, Martha (Paola) Vera-Licona, John Wagner, Xingzhou Yang.

Workshop 5: Uncertainty in Ecological Analysis
April 3-6, 2006

Organizers: Catherine Calder (Department of Statistics, The Ohio State University), Jim Clark (Department of Biology, Duke University), Noel Cressie (Department of Statistics, The Ohio State University), Jay Ver Hoef (Alaska Department of Fish and Game), and Chris Wikle (Department of Statistics, University of Missouri)

Overall Summary

The field of ecology is becoming increasingly aware of the importance of accurately accounting for multiple sources of uncertainty when modeling ecological phenomena and making forecasts. This development is motivated in part by the desire to provide an accurate picture of the state of knowledge of ecosystems and to be able to assess better the quality of predictions of local and global change. However, accounting for various sources of uncertainty is by no means a simple task. Ecological data are almost always observed incompletely with large and unknown amounts of measurement error or *data uncertainty*, and often the expense of data collection prohibits collecting as much data as might be desirable. In addition, most ecological phenomena of interest can only be studied by combining various sources of data; aligning these data properly presents interesting statistical challenges. While data play a large role in most ecological analyses, incorporating scientific knowledge into the analysis through substantive modeling of ecological processes is essential. Often such theoretical contributions are based on competing scientific theories and simplifications of reality. This results in an additional source of uncertainty termed *model* or *process uncertainty*. Finally, substantive models should acknowledge *parameter uncertainty*. For example, more realistic descriptions of ecosystems might allow parameters to vary over space and time. Parameter uncertainty can be handled via empirical or fully Bayesian statistical methods.

The aim of this workshop was to present a thorough investigation and discussion of the various sources of uncertainty that typically play a role in ecological analyses and of the statistical techniques that enable proper inferences and predictions to be made in light of these uncertainties. Concepts were illustrated using new data sources and sophisticated modeling tools developed for studying a diverse collection of ecological phenomena. In addition, there was discussion of strategies for reducing some of the sources of uncertainty including improved design of monitoring networks. The discussion promoted increased communication between the theoretical and empirical statistical/ecological communities. One of the largest communities to use these methods for important decision-making is state and federal governments, and their representatives were involved in the workshop as well.

Summary of Presentations

Day 1

The workshop started with opening remarks by Avner Friedman and Noel Cressie (Director of the Program in Spatial Statistics and Environmental Sciences (SSES), The Ohio State University). Dr. Cressie also gave an introductory talk on Uncertainty in Ecological Analysis. This was followed by methodology overviews on classical statistical methods presented by Byron Morgan (University of Kent) and on Bayesian statistical methods by Mark Berliner (The Ohio State University).

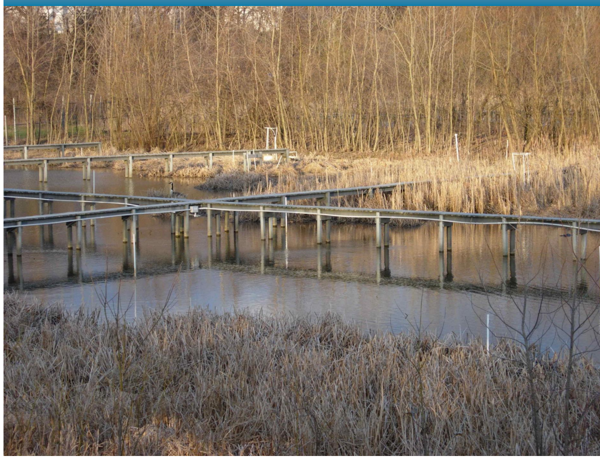
In the afternoon, Jay Ver Hoef (NOAA National Marine Mammal Lab) introduced the ecological study that provided the theme for the break-out discussion groups. The groups met for the first time after Dr. Ver Hoef's introduction to the material. Late afternoon presentations were made on Modeling in the Presence of Uncertainty by Alan Gelfand (Duke University) and Jay Breidt (Colorado State University). A discussion was then led by Jennifer Hoeting (Colorado State University) and Lance Waller (Emory University).

Day 2

The opening session was on Population Dynamics and the speakers were Brian Dennis (University of Idaho) and Steve Buckland (University of St. Andrews). This was followed by a discussion led by Michael Lavine (Duke University) and Mark Maunder (Inter-American Tropical Tuna Commission). After a short break, three new researchers gave presentations: Shannon Ladeau (Smithsonian Environmental Research Center), Devin Johnson (University of Alaska-Fairbanks), and Jarrett Barber (Montana State University). This was followed by the second round of break-out discussions on the ecological study introduced on Monday.

The afternoon session focused on Abundance Estimation with speakers William Link (USGS), Andrew Royle (AMAT/USGS), and Robert Dorazio (University of Florida). A discussion was then led by Ken Burnham (Colorado State University) and Chong He (Virginia Tech).

Tuesday afternoon ended with Jim Clark (Duke University) giving the Workshop Keynote Address, which was also part of the Department of Statistic's Seminar Series. Dr. Clark's talk was titled "Emerging Capacity to Synthesize Data and Process: Application to the Biodiversity Paradox." In this talk, he discussed why the inconsistent assumptions of 'theoretical' and 'statistical' models lead to a paradox. He suggested that coexistence is best understood in terms of population heterogeneity, which may occur along many axes, and is missed by current modeling approaches. By providing a consistent treatment of information from many scales and complex, interacting processes, the Bayesian



approach allows estimation of each of these influences.

In the evening, the Program in Spatial Statistics and Environmental Sciences (SSES) held a reception at the OSU Schiermeier Olentangy River Wetland Research Park. Remarks were given by Doug Wolfe (Chair of the Department of Statistics at Ohio State) and Bill Mitsch (Director of the Wetland Research Park). Tours were given of the facility and the experimental wetland (See page ??? for more information).

Day 3

The morning topic was Spatial Patterns and Processes. The speakers were Marie-Josee Fortin (University of Toronto) and Chris Wikle (University of Missouri-Columbia). The discussion that followed was led by Subhash Lele (University of Alberta) and Philip Dixon (Iowa State University). After a short break, Mevin Hooten (University of Missouri-Columbia), Kiona Ogle (Princeton University), and Bret Elderd (University of Chicago) gave presentations. This was followed by the third round of break-out discussion on the ecological study introduced on Monday.

The first topic for Wednesday afternoon was Community Ecology with speakers Aaron Ellison (Harvard University), Brian Beckage (University of Vermont), and Rachel Fewster (University of Auckland). Then the discussion was led by Tony Ives (University of Wisconsin-Madison) and Robert Dorazio. The next topic revolved around Complexity in Ecosystem Analysis, with presentations by Gabriel Katul (Duke University) and Steve Wofsy (Harvard University). Discussion was led by Doug Nychka (National Center for Atmospheric Research) and Donald De Angelis (University of Miami).

At the Workshop dinner, each leader of the break-out discussion groups gave a short presentation of the outcome of their discussions. This was both enlightening and entertaining.

Day 4

On the last day, there was a panel discussion led by Alan Gelfand, Mark Kaiser (Iowa State University), Michael Lavine, Subhash Lele (University of Alberta), and Jay Ver Hoef, followed by a general discussion. The closing presentation was on Uncertainty in Ecological Analysis: a Retrospective, given by Marc Mangel (University of California).

Conclusion

The organizers changed the format slightly from the usual one used by the MBI. The workshop was shortened by a day, and this kept the intensity of discussion at a high level. A dataset from an ecological study was released to participants, and it was discussed in three breakout discussion groups with each group's summary being given at the workshop dinner. This gave participants something to discuss that was focused on data and the associated ecological study; discussion occurred formally in groups and informally during breaks and social occasions.

In summary, the workshop provided an opportunity for the ecological science community to interact with the statistical and abstract-modeling communities. It promoted novel, interdisciplinary research developments on complex models, inference, and design in the face of various sources of uncertainty.

Wetlands Tour

As part of MBI Workshop 5 on Uncertainty in Ecological Analysis, the Program in Spatial Statistics and Environmental Sciences (SSES) held a reception on Tuesday, April 4th, at Ohio State's Schiermeier Olentangy River Wetland Research Park. This 30-acre park, located just north of campus, is one of the premier wetland research and education facilities in the nation. It was established by William Mitsch, Professor of Natural Resources and Environmental Science; Mitsch currently serves as director of the facility. The research park consists of two 2.5-acre deepwater marshes and a river water delivery system, both completed in 1994. Additional wetlands and microcosms were added to the park in 1999.

The reception was held in the park's 9,000 square foot Heffner Wetland Research and Education Building, and guests were given guided tours led by Mitsch and several graduate students. In addition to the workshop participants and MBI affiliates, faculty from the Department of Statistics and SSES associates attended the event. Remarks were given by Mitsch, Noel Cressie (Director of SSES), and Doug Wolfe (Chair of Statistics).

Workshop 6: Microbial Ecology
May 15-19, 2006

Organizers: George Jackson (Department of Oceanography, Texas A&M University) and Frede Thingstad (Department of Microbiology, University of Bergen)

Overall Summary

A description of microbial ecology is complicated by the fact that microbes occur in many different environments, mostly terrestrial and aquatic, and that microbes include autotrophic as well as heterotrophic organisms. Further complicating organization of a small meeting on microbial ecology is that theoretical microbial ecology is done in multiple disciplines whose interactions are weak.

Classical ecology tends to emphasize structural issues, such as

- What controls the numbers, species, and distributions of microbes?
- How are these manifested in genetic diversity?

Aquatic ecologists have been influenced by chemists and physicists. Their questions tend to revolve to be similar to

- What determines the rates of energy and material processing?
- What are the mechanisms by which microbes interact?
- How does the environment structure these?

The goal of the meeting was to bring together leading researchers from these different approaches together. The speakers also included researchers exploring innovative ways to use observations to infer system properties by, among other means, using new statistical approaches.

Summary of Presentations

Day 1

The first substantive talk was by Jim Grover (University of Texas at Arlington), who focused on the the role of elemental stoichiometry in microbial food webs. The law of mass conservation constrains the dynamics of interacting microbial populations. These stoichiometric constraints facilitate theoretical studies of how species interactions relate to dynamics of nutrients and other substances. In theory, stoichiometry affects the coexistence and stability of populations interacting through mechanisms such as competition for resources, allelopathy, commensalism, mutualism, and predation. Experimental studies support many predictions of stoichiometric theory as applied to interacting microbial populations. Stoichiometric signatures are also

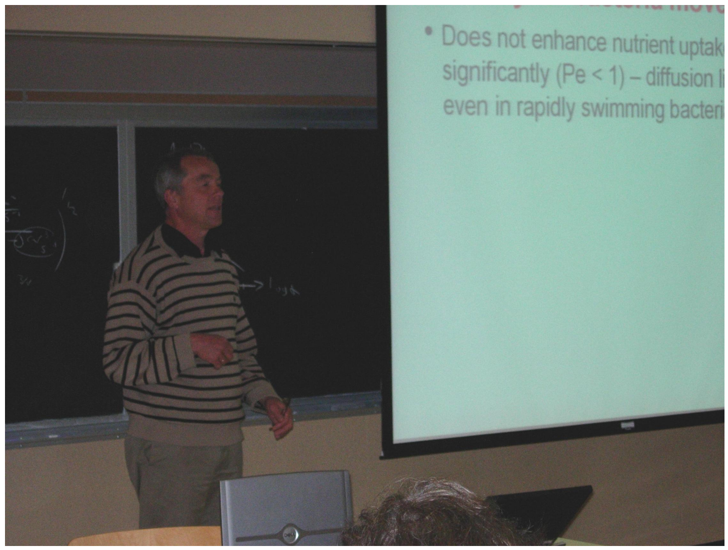
predicted for the assembly of diverse communities. Although existing theory is largely limited to steady state analyses of systems with two growth-limiting substances, current research extends the stoichiometric approach to three growth-limiting substances and non-steady conditions.

After lunch, Jarl Giske (University of Bergen) discussed the use of individual-based models (IBMs) and the incorporation of evolutionary approaches to determine decisions and behavior, discussing work performed in conjunction with his colleagues, Fred Thingstad and Espen Strand. At the outset of population modeling, an individual was seen as a number among other equals in the population. Later, extensions have been introduced to account for individual variability within population models. These extensions may be classified into community ecology models, game theory, state-dependent models, and age-dependent models. Jarl showed that the individual-based approach can be used to merge these traditions. Furthermore, the ING concept and hedonic modeling can be used to combine genetic variation and density- and frequency-dependency with trade-offs linked to age and state. Jarl showed how the simulations of evolution in a microbial community can be used to test various strategies of autotrophy and mixotrophy.

Mike Dowd (Dalhousie University) followed with a presentation on statistical data assimilation as it is used in ocean biogeochemistry. Estimating the time evolution of ocean biogeochemical variables requires both models and data. Mathematical models for ocean biogeochemistry are based on nonlinear (ordinary and partial) differential equations, and exhibit complex dynamical behavior and high dimensionality. Observations come from a variety of sources and are characterized by being noisy, sparse, and non-Gaussian, and with complex spatial and temporal structure. Mike's talk considers some emerging statistical approaches for estimating the time evolution of the biogeochemical state of the ocean (along with relevant parameters). These use a state space framework, which incorporates nonlinear (stochastic) dynamical models and available data. Solutions are probabilistic and rely on sampling based (sequential Monte Carlo) methods. Application and illustration of these approaches is presented using models of pelagic ocean biogeochemistry (e.g., PZND models: phytoplankton, zooplankton, nutrient, and detritus).

After extensive discussions, the group moved to examine poster presentations. Daniel Dougherty (Michigan State University) presented his work on modeling the effect of diffusive processes on ionic strength inside a cell's membrane and how it affects reactivity. Markus Pahlow (Dalhousie University) and Laurent Arnaud (CNRS) presented work they are doing on modeling phytoplankton blooms in a bay south of Halifax, Canada. One of their goals is to keep both the biology and the physics no more complicated than necessary to explain observations. Fabien Lombard presented his experimental and modeling work on ciliates-appendicularian interactions. It was done in collaboration with D. Eloire, A. Gobet, A. Sciandra, L. Stemmann, J. Dolan, and G. Gorsky. He developed models of feeding by ciliates and by appendicularians when the two were raised separately. When applied to organisms that are reared together, growth rates for both groups were higher than predicted. This suggests that there are advantages for both organisms in the interaction. Ciliates seem to be parasites of appendicularians houses where they can find high concentration of food, whereas large appendicularians may ingest ciliates. These hypotheses were confirmed afterward by microscopic observations, and we propose a description of the different interaction based on appendicularians size.

Day 2



Tom Curtis (University of Newcastle upon Tyne) discussed the use of neutral community models to understand microbial diversity and community assembly. He presented work done in collaboration with colleagues Mary Lunn, Stephen Woodcock, and William T. Sloan. The nature and extent of bacterial diversity is a frontier in science of astronomical dimensions and profound practical importance. Bacterial diversity is unknown at any scale in any environment. Debates about the nature of a species contribute to but do not actually cause this confusion. Rather the scale and inscrutable nature of the microbial world, combined with a paucity of theory, prevents us from gaining a clear picture of bacterial diversity. For example, in most environments we are confronted with exponentially increasing numbers of taxa at exponentially decreasing abundances. Random sampling often reveals the same taxa again and again and we cannot therefore distinguish between rarity and absolute lack of taxa. Unfortunately, sample sizes are dictated by budgets not statistics. The usual alternative to counting is to infer the numbers from a taxa abundance curve, which one can either guess or infer by fitting curves from samples. Alas, the biggest samples are very small with respect to the community and the fitted parameters can be so uncertain as to yield quite variable estimates of diversity. Nevertheless, theory can lend a hand. We believe that fundamental, and hopefully universal, aspects of community assembly can be expressed mathematically, and that therefore diversity can, in principle, be predicted. Unfortunately, these predictions must be made in a world we can barely perceive and in which meaningful quantitative studies are expensive, laborious, and prone to failure. Consequently, complex and unparameterized models must be eschewed for they are potentially very misleading. We need a theory that is simple and amenable to calibration using small samples. In our hands, stochastic, birth death, and invasion models can fulfill this role (especially if they can be complemented by deterministic models to determine the number of individuals). These neutral models are conceptually analogous to MacArthur and Wilson's "Theory of Island Biogeography" and will describe, inter alia, taxa abundance curves, and thus diversity. Theory is not a substitute for the empirical measurement of diversity but it could prove an invaluable ally in this task. It will allow us to design the large scale sequencing programs that are required for definitive studies on microbial diversity in some communities, which could in turn permit the confident prediction of bacterial diversity in others.

Åke Hagström (University of Kalmar) presented the results of his work to understand microbial distributions. For most eukaryotic organisms a species is defined as an interbreeding population. However, bacteria do not have sex. Instead they acquire DNA fragments for recombination in several direct ways (i.e., horizontal gene transfer). Thus, the traditional Biological Species concept makes little sense in relation to bacterial speciation. To overcome this problem the concept of ecotypes defined as populations of bacterial cells that show genetic cohesion and are ecologically distinct has been introduced. In his presentation, Åke discussed the "species" issue in relation to current estimates of total marine bacterioplankton diversity. Also, bacterial cosmopolitanism, widely accepted by microbiologists, confronts recent reports of endemic species and restricted distributions. Because of their small size, huge abundance and easy dispersal, it is assumed that marine planktonic microorganisms may show a ubiquitous distribution that prevents any structured assembly into local communities. Currently, a global picture of the bacterioplankton distribution in surface layer is emerging, showing a marine bacterioplankton community that follows a latitudinal gradient of diversity and that includes few truly cosmopolitan species. The structure of the bacterioplankton community that leads to these results was discussed as well as the implications of a structured bacterioplankton community for modeling biogeochemical cycles in the ocean.

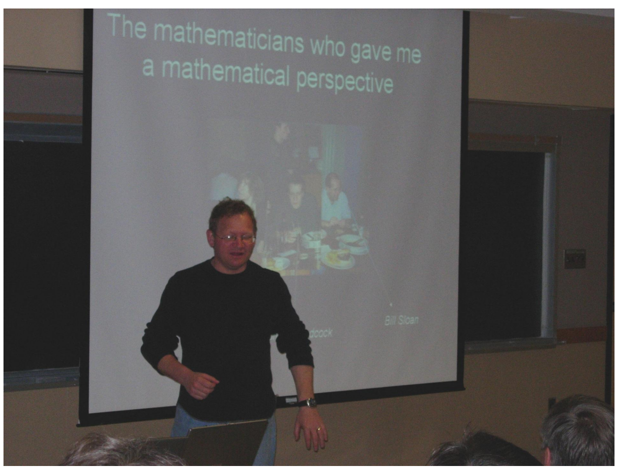
After a lunch break, Mary Lunn (St. Hugh's College) focused on the issue of actually fitting data to distributions and the role of simulations. Given huge populations of microbes, extracting as much information as possible from small subsamples is important. Analytic methods based on traditional likelihood calculations are difficult to use when selecting a subsample from a potentially large number of species. Mary presented some preliminary results on how simulation may be used, applying the method to data from soil and human gut flora.

Andy Visser (Danish Institute for Fisheries Research) moved the discussion into a more mechanistic direction when he discussed encounter rates in the plankton and the roles of motility, turbulence, and sensory ability. For planktonic organisms, nearly all important life processes are governed by an encounter rate. For instance, growth, reproduction, and mortality are closely linked to an individual's encounter with food, mates, and predators respectively. Understanding the distribution of resources on scales relevant for individual organisms, and how they locate and exploit these resources is central to understanding how marine ecosystems function. At these scales, the dispersion of material is controlled by molecular diffusion, turbulent straining, and Richardson's law. That is, the landscape experienced by plankton (i.e., chemical patches, detrital aggregates, and other organisms) is strongly controlled by small scale physics. Lagrangian models of planktonic interactions can be built up by examining (i) their small scale physical environment, (ii) their motility and behavior, and (iii) their sensory ability in remotely detecting each other and patchily distributed resources. As an example, many aquatic organisms - from bacteria to crustaceans - use chemical plumes released by sinking particulate organic material either directly as a food source or as a signal to find potential food items (marine snow aggregates, fecal pellets). This interaction is important as it determines where, how fast, and to what degree sinking detrital material is demineralised in the water column; a pivotal process in determining the vertical carbon flux in the ocean. This example highlights the interplay of abiotic aspects of the environment, in particular turbulence, with the sensory ability and motile behavior of planktonic organisms.

There were several short talks on days 2 and 3 by people attending the meeting but who were not giving scheduled lectures, including Raechel Waters (University of Washington), Maayke Stomp (University of Amsterdam), Hans-Peter Grossart (Institute of Freshwater Ecology & Inland Fisheries), and Oliver Ross (University of Essex).

The day ended with a public lecture by Thomas Kiørboe (Danish Institute for Fisheries Research) entitled *Blind dating: the secret life of pelagic copepods*. The talk emphasized the importance of individual mechanisms of interaction between aquatic organisms and how they place important constraints on organism populations.

Day 3



Laurent Seuront (CNRS) presented the microscale distribution of microbes and the challenges it poses to theories of ecological complexity. A ubiquitous feature of aquatic ecosystems is the temporal variability and spatial heterogeneity that occur over a wide range of scales. Despite the considerable amount of work devoted to the quantification of the spatial and temporal patterns of plankton distributions, their intrinsic three-dimensional and microscale properties have widely been underestimated. Using tools borrowed from the field of statistical physics, Laurent illustrated how taking into account the space-time complexity of microbial distributions at microscale and in 3D, in particular their intermittent behavior and the related dynamics of extreme events, can provide extremely valuable ecological information. He paid specific attention to the nature of and the interplay between turbulence intermittency, seawater viscosity, individual swimming and mating behavior, and predator/prey and virus/host interactions.

Next, Thomas Kiørboe discussed particle associated microbial communities in pelagic environments, emphasizing their dynamics and significance. Rich microbial communities develop on and around suspended particles in pelagic environments. Their activity may account for a significant fraction of the microbial activity in the water column and they enhance the degradation of sinking particles, thus retarding vertical material fluxes in the ocean. Thomas used a combination of simple mechanistic models and experiments to explore the dynamics of these communities. The description considered motility behavior and colonization of bacteria and flagellates, growth and detachment of particle-attached microbes, and trophic interactions. The models and experiments are capable of describing some gross features of particle-attached microbial communities, such as how the abundances of attached microbes scale with particle size, but there are many open and unresolved questions. These include the similarity or difference of particle-attached and free microbes; the interaction between the dynamics of the particles (as they form and degrade) and the dynamics of the microbes; and the significance for ocean carbon fluxes of these microbial communities.

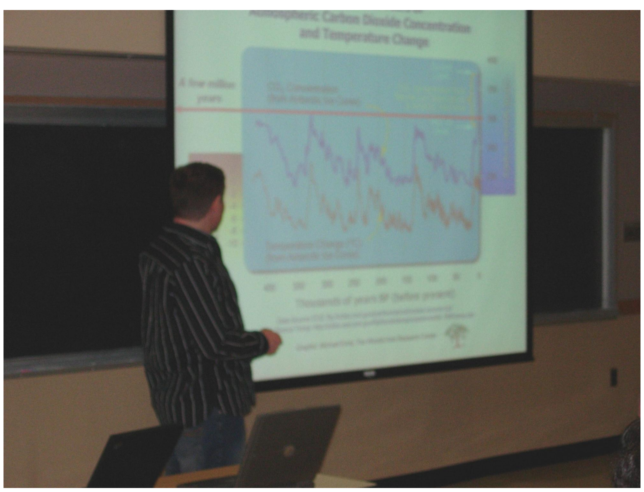
Dick van Oevelen (Centre for Estuarine and Marine Ecology) discussed how the role of bacterial carbon in marine benthic food webs can be studied by integrating experimental 13C isotope data with models. Bacteria dominate biogeochemical processes in most sediments. Bacterial production and respiration processes are therefore studied in detail by biogeochemists. However, the fate of produced bacterial biomass is often not considered. The ubiquitous presence of bacteria, their high nutritional value and secondary production has lead many benthic ecologists to speculate that bacteria fulfill an important carbon transfer in the benthic food web. Recent evidence suggests that viral infection and subsequent lysis may be an important factor in bacterial loss processes in the pelagic zone, but its significance in sediments is not well established. It is clear that an integrated approach is required to understand the dynamics of bacteria in sediments. Dick presented the result of an in situ experiment, in which 13C-glucose was injected 10 cm into the surface of a marine intertidal sediment, and which was analyzed using a model. The project also involved Leon Moodley, Bart Veuger, Karline Soetaert, Jack J. Middelburg, and Carlo H. R. Heip as collaborators. The injected 13C-glucose was quickly incorporated by the bacterial community as evidenced by 13C enrichment of bacterial specific biomarkers (polar-lipid-derived fatty acid and D-alanine) and its fate in the food web was followed during a period of 4.5 months. Trophic transfer through grazing on bacteria was assessed through the 13C enrichment of meio- (group level) and macrobenthos (species level). Respiration was monitored through the production of 13C dissolved inorganic carbon. 13C enrichment of different sedimentary amino acids was used to gain insight in preservation of bacterial remnants in the particulate organic carbon pool of the sediment. The complete data set was evaluated with a mechanistic model to quantify the importance of exchange processes (i.e., resuspension and irrigation), bacterial grazing by benthic fauna and bacterial growth, respiration, and mortality. The interaction between bacterial and benthic fauna can be viewed from the bacterial perspective in terms of the importance of grazing as a fate of bacterial carbon production. Another interesting question is how much the grazed bacterial carbon contributes to the total carbon requirements of benthic fauna. To address this question, the relative enrichment of meio- and macrobenthic taxa was evaluated against the relative enrichment in bacteria by means of a simple isotope model. He used Bayesian analysis in both modeling approaches to determine the constraining effect of the data - model interaction on the model parameters.

In the second talk of the afternoon, Alain Vézina (Bedford Institute of Oceanography) talked about the use of inverse models and the parsimony principle in investigations of microbial food webs. Microbial food webs are maintained by complex flows of carbon, nutrients, and biochemical compounds that cannot be fully quantified by measurements. Inverse modeling was introduced to biological oceanography and microbial ecology in the late 1980s as a way to reconstruct complete flow networks from incomplete information. The reconstructed flow network is the simplest among all plausible configurations. In other words, it is the flow network that contains no more structure than is required to explain the data. This parsimony principle has implications for the reconstructed microbial interactions that are not always realistic. This lecture will review new approaches to counter adverse effects of the parsimony principle and possible approaches to replace it completely. At this time it appears that parsimony will remain an integral part of inverse analysis but recent improvements in inverse modeling promise to decrease its impact on the results.

At the end of the day, Hao Wang (Arizona State University) made a brief presentation of his model for the Japanese lake Biwako. He was interested in the relationship between bacteria and algae. The bacteria compete with the algae for inorganic nutrients such as phosphorous but rely on them for organic carbon.

Day 4

Mark Moore (University of Essex) discussed the physiological basis for modeling productivity in the sea. This was a result of collaboration with Richard Geider. Photosynthesis in the oceans is dominated by phytoplankton, an assemblage of organisms spanning many phyla across 2 empires. In addition to this vast genetic (adaptive) variability, phytoplankton have evolved a large capacity for physiological plasticity (acclimation). Modeling the response of primary productivity to environmental forcing thus potentially represents a major challenge. Mark addressed how to confront this challenge from a mechanistic physiological view point. Initially he considered slower timescale acclimation to temperature, light, and nutrient availability, modeled in terms of adjustments in cellular constituents acting to balance the supply of energy through photosynthetic light capture, with the electron demands for biosynthesis and maintenance. Changes in the cellular chlorophyll to carbon ratio capture the essence of these models, which are likely to provide a reasonable approximation of phytoplankton photosynthesis in stratified conditions. In contrast, rapidly mixed layers often characterize the regions of the upper ocean where the highest productivity occurs (e.g., mid-high latitudes during spring). Understanding the physiological response to the high frequency variations in light occurring in this situation will likely require consideration of faster kinetic processes. Potential means of modeling these “energy modulation” processes, which include both non-photochemical quenching and photoinhibition, will be described. A key challenge is to scale back up from these physiological models to ecosystem and global scales.



Danny Grünbaum (University of Washington) presented the issue of plankton patchiness and how it causes a disconnection when using laboratory data on feeding rates as a function of food concentration to infer feeding rates in the field.

Jef Huisman (University of Amsterdam) started the afternoon off by talking about mixing and chaos in plankton communities. Physical mixing processes have a major impact on species interactions in plankton communities. Jef developed a theory to predict how changes in turbulent mixing affect the population dynamics of phytoplankton species. He applied the theory to two contrasting aquatic ecosystems, a hypertrophic lake, and the oligotrophic ocean. In hypertrophic lakes, where nutrients are in ample supply, the growth rates of phytoplankton species are often limited by light availability. The light conditions experienced by phytoplankters depend on their vertical excursions through the water column. To investigate how changes in vertical mixing affect competition for light between different species, we manipulated the turbulence structure of an entire lake using artificial mixing. Changes in turbulent mixing of the lake caused a dramatic shift in phytoplankton species composition. Consistent with Jef's model predictions, sinking diatoms and green algae dominated during intense mixing, while buoyant and potentially toxic cyanobacteria became dominant when mixing was reduced. In the oligotrophic ocean, phytoplankton species face two opposing resource gradients: light supplied from above and nutrients supplied from below. As a result, phytoplankton cells may achieve highest growth rates not at the water surface, but at a depth where both resources are available in sufficient supply (i.e., a deep chlorophyll maximum develops). Jef's model predicts that reduced vertical mixing, which brings less nutrients into the euphotic zone, will generate oscillations and chaos in the phytoplankton of the deep chlorophyll maximum. These intriguing model predictions are compared with the complex species dynamics observed in deep chlorophyll maxima of the subtropical Pacific Ocean, as revealed by long-term studies of the Hawaii Ocean Timeseries program. According to recent climate models, global warming will lead to a stronger vertical stratification of lakes and oceans, which reduces vertical mixing in the water column. The results of our plankton models, lake experiments, and ocean observations warn that changes in the vertical mixing structure, driven by climate change, can induce major shifts in the population dynamics and species composition of phytoplankton communities.

Joe Vallino (Marine Biological Laboratory) asked the question of whether non-equilibrium thermodynamics govern metabolic network expression in microbial communities. He took a metabolic perspective of ecosystem biogeochemistry that functions at local, region and global scales, in deep-sea hydrothermal vents and the deep biosphere, as well as in laboratory microcosms. In all these systems, a complex metabolism governed by microorganisms develops; however, instead of the metabolism being orchestrated by a single organism, metabolic function is distributed among hundreds of microbial species, yet the overall system-metabolism functions in a highly organized and coordinated manner. What governs the development and organization of this distributed metabolism? Is it governed by just happenstance depending on which organisms are present in the system at a particular instance, or are there fundamental governing laws that dictate how the system metabolism will develop? It has been hypothesized that 3.5 billion years of evolution has produced biological systems so adept and efficient at producing and degrading chemical potential that the overall biogeochemistry of microbial systems can be accurately described by simple rules without requiring knowledge of the individual species that occupy a given system. Accordingly, the biogeochemistry observed on Earth, at both local and global scales, may be governed by principles derived from nonequilibrium thermodynamics with living systems being the mechanism by which the system attempts to degrade energy gradients. Using a distributed metabolic perspective constrained by nonequilibrium thermodynamics, Joe presented a modeling framework that can predict ecosystem biogeochemistry assuming the system is sufficiently metabolically diverse. The model predicts how resources (i.e., carbon sources, nutrients, chemical electron acceptors, and donors) change over time, as well as how the overall system allocates protein to metabolic processes, such as photosynthesis, nitrification, sulfate reduction, respiration, etc., as governed by the principle of maximum entropy production (MEP). The primary research objective is to demonstrate, via model comparison to experiments, that living systems tend to track the MEP objective. He presented development of the modeling framework that incorporates thermodynamic objective functions as well as model comparison to preliminary microcosm experiments in which state and microbial compositions are monitored.

After the last talk of the day, there were two panel discussions:

- The first panel was composed of the speakers whose work involved the use of advanced statistical techniques to compare experiment results with models and the approaches that look promising for the future. Panelists included Mike Dowd, Mary Lunn, Dick van Oevelen, Alain Vézina, and Tom Anderson. There was agreement that Monte Carlo Markov chains offer a significant improvement over earlier techniques.

- The second panel was composed of mathematicians attending the workshop, Joe Mahaffy (San Diego State University) and Hal Smith (Arizona State University). While they were asked to provide mathematicians' responses to the work present to date, the discussion veered off to discuss approaches to making mathematics approachable to biologists.

Day 5

Bernie Boudreau (Dalhousie University) started the morning, as he explored the relevance of biological models of microbial systems for the description of chemical transformations in the benthos. Most biogeochemical changes that occur to sediments after their deposition are related to organic matter decomposition, which is a microbial process. Transport-reaction modeling of this diagenesis has been extremely successful at describing and explaining the resulting distributions of solid and solute components of sediments. Bernie highlighted these successes, focusing on examples from microbial mats and the transient redistribution of redox-sensitive metals. A surprising result from this modeling, confirmed by experimental results, is that the microbial population need not be modeled explicitly. He then explored the theoretical basis for this seemingly contradictory finding. Finally, he examined the feedback between the macro-fauna and the microbial population in sediments.

Pete Jumars (University of Maine at Orono) presented the results of a collaboration (with K.M. Dorgan, B.P. Boudreau and B.D. Johnson) that examined the nature of unsteady environments of benthic marine microbes. Bacteria in sediments exist at a surprisingly constant

10^9 individuals ml^{-1} of pore water. However, every indication is that the majority of those cells are idle most of the time. Messenger compounds are one means to signal that renewed metabolic activity would be worthwhile, and signals sent or received this way have some interesting features in an environment containing diffusion-reflecting boundaries. Mechanical stresses in sediments have received less attention, but new models and measurements in sediments and sediment analogs suggest that many muds behave mechanically like linear-elastic, solid gels with fairly simple large-scale geometries. Burrowing animals produce stress and strain fields in them and fracture sediments. These stress-strain and fracture fields can provide direct mechanical stimuli and can have large influence on solute delivery by short circuiting otherwise diffusively delivered chemical signals.

Conclusion

Discussions with the participants suggested that the meeting had achieved its goal of exposing members of the different ecological communities to each others work. The discussions after talks were frequent and stimulating. Furthermore, the personal interactions that developed among participants after a week of interactions offer the chance that the interactions will continue in the future.

Workshop 7: Global Ecology
June 26-30, 2006

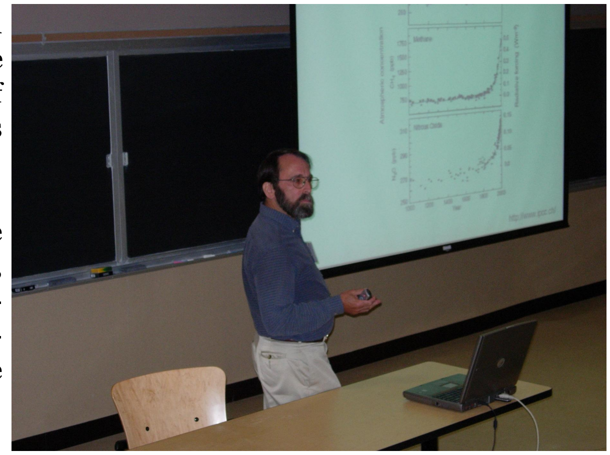
Organizers: John Harte (Energy and Resources Group, University of California), John Pastor (Natural Resources Research Institute, University of Minnesota), and David Schimel (Climate and Global Dynamics Division, National Center for Atmospheric Research)

Overall Summary

The globe is warming because humans are adding carbon dioxide and other radiatively active gasses to the atmosphere through fossil fuel combustion, land use change, and application of vast amounts of fertilizer. The global system responds to these alterations to its carbon and elements cycles and the climate through a set of feedbacks, both positive and negative. Understanding how the earth works as an integrated system, especially in response to anthropogenic perturbations, poses many mathematical and ecological challenges that were explored in this workshop.

The workshop brought together some 48 participants, including mathematicians and ecologists and senior researchers and graduate students. It consisted of two to three formal talks in the mornings, which presented the mathematical challenges underlying several important ecological questions. The afternoons were devoted to discussions, tutorials, and short talks exploring some topics in more depth.

Formal Talks



Three talks Monday morning set the general picture for the week. John Pastor opened the workshop with a survey of major problems of global ecology and the mathematical challenges they pose. These included:

- General behaviors of energy flow and the carbon cycle as coupled dynamical systems, especially how bifurcations between different equilibria arise from critical combinations of parameter values that determine their fluxes.
- Stochasticity and noise in parameters.
- Stoichiometric coupling between element cycles and how this affects trajectories and stability of solutions.
- Scaling of rates to different spatial and temporal domains.

John Harte followed and discussed the role of terrestrial biota in controlling carbon cycles and the climate system. Harte showed that the known fluctuations in the ice core CO_2 and temperature records cannot be explained without invoking positive feedbacks with biota and that these feedbacks probably arise in the fine dynamics of individual species responses to their environment. Rob Armstrong (SUNY at Stony Brook) then turned out attention to the ocean systems and the chemistry of carbon dioxide and carbonate ion species in the oceans. Increased atmospheric CO_2 concentrations also cause dissolved carbonic acid concentrations in the oceans to rise. This in turn could easily cause the pH of the oceans to switch rapidly from slightly basic to acidic making the forming of carbonate shells by mollusks and corals problematic. The emerging theme of these talks was that once critical thresholds of parameters are crossed, positive feedbacks can rapidly take the system from one equilibrium or basin of attraction to another.

These rapid responses of the global system to critical parameter values appear similar to bifurcations in dynamical systems models, which were explored on Tuesday morning. Ray Pierrehumbert (University of Chicago) opened Tuesday's sessions by discussing the co-evolution of biota and the earth's climate systems, especially the transition from a very warm Early Earth with an atmosphere dominated by methane, an even more powerful greenhouse gas than CO_2. Once organisms that can engage in oxygenic photosynthesis evolved, the world's climate cooled considerably, even precipitating one or more Paleoproterozoic snowball

Earth episodes. With the evolution of vascular land plants, silicate weathering increased, which in turn sequestered carbon dioxide in weathering products, leading to a cooler climate. Bruce Peckham (University of Minnesota) followed and presented a dynamical systems model of element fluxes in peatlands. Peatlands contain 1/3 of all the carbon sequestered in the world's soils since the last deglaciation and are therefore important carbon sinks. The model shows that different peatland plant communities are separated by transcritical and Hopf bifurcations that depend on critical balances of inputs and outputs of limiting nutrients such as nitrogen. Barb Bailey (University of Illinois) finished the morning by discussing how noise affects the behavior of dynamical systems. She presented methods by which the dimension of a system, the nature of its attractors, and the sign and magnitude of Lyapunov exponents can be inferred from analysis of time series using nonlinear regression. She first applied these techniques to reconstruct the Lorentz attractor from a noisy time series, then applied these methods to a stochastic model of carbon fluxes in coupled phytoplankton-zooplankton systems.

Wednesday morning was devoted to exploring the stoichiometric couplings between carbon cycles and those of other elements such as nitrogen and phosphorus. Bob Sterner (University of Minnesota) opened the day with a discussion of Redfield ratios in marine and lacustrine plankton and how these ratios constrain carbon uptake rates. A key feature of these couplings is the homeostatic regulation of internal ratios in organisms. Some organisms have very tightly regulated internal element ratios, whereas the internal ratios of others respond quite rapidly to that in their surrounding environment. The first set of organisms can exert greater control over element cycles than the latter. Chris Klausmeier (Michigan State University) followed by presenting a dynamical system model of coupled element cycles in the oceans, which showed that the Redfield ratios are not constant but vary widely, depending on parameters that control fluxes between trophic levels. Irakli Loladze (The Ohio State University) finished the morning by presenting a statistical analysis of a large empirical database on how plant C: element ratios respond to higher CO_2 concentrations, especially for food plants. These analyses suggest that higher CO_2 concentrations lead to reductions in nutritional quality of foods.

On Thursday, Dave Schimel (National Center for Atmospheric Research) and Gabriel Katul (Duke University) explored mathematical challenges of scaling measurements made at one level to larger spatial and longer temporal scales. Schimel presented new techniques of model inversion to reconstruct system structure from time series of records, such as detailed time series of CO_2 from eddy correlation towers. Katul analyzed a soil moisture-evapotranspiration model using Fourier and wavelet techniques and showed that 99.6% of the soil moisture variance could be described by less than 0.4% of the Fourier modes, suggesting considerable simplification of hydrologic models.

Discussions and Tutorial Sessions

Day 1: Afternoons were devoted to discussions and tutorial sessions. Participants discussed how to improve graduate education of ecologists in the mathematical sciences in order to better address problems of global change. The participants came up with a list of mathematical techniques that they use routinely and that they felt graduate students should have a working familiarity with. These range from eigenvalues, stability analysis, and other techniques of dynamical systems to Fourier, wavelet, and other statistical techniques of analyzing time series of data to model inversion techniques. The participants recognized that no one is expert in all these techniques, but that close familiarity with at least a few prepares the student for learning the others on their own as they are needed. The participants each chose one of these techniques and are writing a paragraph on each with key references; these paragraphs will be compiled into a paper which could be submitted to a journal such as Frontiers of Ecology.

Day2: Yosef Cohen (University of Minnesota) led a tutorial session using Mathematica on modeling evolution under a changing climate. The techniques involved describing a parameter of a coupled differential equation model of several interacting species as a frequency distribution which evolves in response to changing forcing function of climate or interactions with the other species in the model (coevolution).

Day 3: Yang Kuang (Arizona State University), John Nagy (Scottsdale Community College), and Hao Wang (Arizona State University) led a tutorial session on modeling predator-prey interactions in a changing climate and how changes in climate could alter population oscillations. The session drew heavily from dynamical systems theory, especially bifurcation theory, to analyze several candidate models.

Day 4: The discussants were asked: What is the single mathematical or computation advance you would like to see that would then allow you to make rapid progress on problems of global change? The suggestions included:

- Develop and prove a theorem for admissible behaviors of ecosystems from a network diagram of their structure and some minimum constraints on their functions (some progress along these lines has been made by Golubitsky and Stewart. 2006. Bulletin of the American Mathematical Society 43: 305-364).
- A method of identifying the structure and parameters of a system from data, especially a time series of important system behavior, such as eddy correlation or other CO_2 flux data.
- What is the simplest widget to add to a model to account for unexplained variance at particular scales?
- A theory or theorem that would relation system structure to time scales of behavior.
- A theory or theorem that would help us identify the manifolds of traits that result in (un)

stable solutions of models.
- A more rigorous model simplification process.
- Describing uncertainty so you call tell what to trust from your model (what is reliable, what is not?).
- What are the rules for splitting data to calibrate and test models?

In addition, several short impromptu papers were presented to cover topics not covered in the longer formal papers presented in the mornings. These papers included pattern formation in ecosystem models (Max Rietkerk, Utrecht University), allometric scaling of carbon fluxes (Andrew Kerkhoff, Kenyon College), model inversion techniques (Anna Michalak, University of Michigan), and extreme N:P ratios in Lake Superior and their implication for input-output budgets (Bob Sterner).

Friday morning was devoted to a warp-up discussion of common themes that seem to cut across the weeks' papers and discussions. These included:

- The coupling of an open energy flux system across the globe with closed element cycles, particularly that of carbon. The open energy system drives the circulation of carbon through the world's biota, but the distribution of carbon amongst different pools affects the energy balance. What are the stabilities and trajectories of coupled open-closed system models?
- The need for an admissible behavior theorem to help us anticipate "surprises" and to focus our attention on what may be allowable. We probably need more than a wiring diagram of system structure, possibly turnover rates of compartments and general functional forms of transfers between compartments, and the theorem may actually specify what is not an admissible behavior.
- The behavior for the globe is complicated by processes that couple several time scales. Photosynthesis occurs at the fastest time scale (minutes) but respiration can be thought of as a lagged carbon flux as carbon passes from photosynthesis through several pools. However, the pool with the slowest turnover (soils and sediments) provides the nutrients that subsidize the fast process of photosynthesis. Stoichiometric constraints also couple fast and slow time scales. General solutions to these problems remain challenging – the usual method is to focus on only a few time scales and treat processes at other time scales and either constants or white noise.
- Because species and processes spread over the globe, time and space scales are coupled, resulting in dynamic spatial patterns. Reaction-diffusion theory provides some formal approaches to this problem, but cellular automata theory is also useful.
- The need for better quantification of system behavior and boundary conditions. The globe has complicated boundary conditions, such as coastlines and mountain ranges, which constrain fluxes of materials and energy. We need to define boundary conditions as functions, not as constants. We also need to look for quantifications that reveal new behaviors rather than simply improve accuracy of predictions.

Conclusion

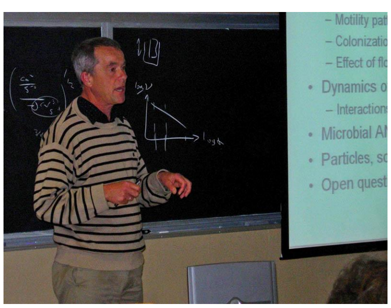
The workshop sparked a number of spirited but friendly discussions throughout the week during coffee breaks and meals. People were able to meet other researchers whom they had never met but whose papers they have read. The small size of the workshop and the expertise of the participants greatly facilitated these informal exchanges, which were perhaps the most valuable part of the workshop. Numerous suggestions were made to the presenters for alternative ways of formulating the problems, for alternative techniques, and to use other computational tools. It is hoped that these interactions will lead to new collaborations and new directions in global change ecology and mathematics. The globe is unlike any constituent ecosystem because it is closed to element cycles but open to energy fluxes – all constituent ecosystems are open to both material and energy fluxes. It is not even clear that the traditional way of dividing the globe into atmospheric, terrestrial, and marine compartments is the best one – perhaps we should be dividing the globe into pools of homogenous turnover rates regardless of location. It was clear from this workshop that new mathematical approaches in dynamical systems theory, stochastic variable theory, and model inversion will greatly increase our understanding of the global system. In addition, the global system provides a great deal of non-trivial motivation for further development of these mathematical theories and techniques and enriches our understanding of the mathematical concepts and objects used to analyze it.

Public Lecture Series

Ransom A. Myers, Killam Chair of Ocean Studies at Dalhousie University, Halifax, Nova Scotia
The Global Loss of Top Predators in the Ocean: Consequences of a World Without Sharks, Tuna, and Great Fish
Tuesday, February 7, 2006

There has been a phenomenal loss of large predators in the ocean; within the last 50 years the abundance of large fish predators has been reduced by approximately 90 percent. Once thought to be the most abundant large vertebrate in the world, the oceanic white tip shark was 300 times more abundant off the coast of the southern United States only 50 years ago than it is today. Dr. Ransom A. Myers discussed the ecological consequences of this loss of predators and how over-fishing has drastically changed the world's oceans.

Recently named by *Fortune* magazine as one of the world's top 10 people to watch, Dr. Myers is an oceanographer with degrees in mathematics, physics, and biology. His current work analyzes data from fish populations, examining each population as a realization of a natural experiment, which has led to the discovery of patterns in nature that have not been seen before. This exciting work offers the possibility of solutions to both theoretical and applied problems in population biology and resource management. Dr. Myers has carried out fundamental work on the causes of the collapse of fish stocks—in particular, the cod stocks in eastern Canada. He has served on the board of directors of the International Oceans Institute of Canada, Ocean Institute of Canada, and the Resource Modeling Association and has been supported by a wide variety of government, industry, conservation, and private foundations.



Thomas Kiørboe, Professor of Marine Ecology and Aquaculture Department at the Danish Institute for Fisheries Research, Charlottenlund, Denmark
Blind Dating: The Secret Life of Pelagic Copepods
Tuesday, May 16, 2006

How do small pelagic copepods manage to find mates in a large 3-dimensional world? Copepods are by far the most important zooplanktons in the oceans and are the main food for pelagic fish and fish larvae. Their population dynamics and abundance are constrained by their capability to find sex partners. With video clips and animations, this lecture will reveal the fascinating mate-finding and courtship behavior of these tiny (millimeter-sized crustaceans. Dr. Kiørboe showed how females signal their presence and position to the males and how the males optimize their search for females. Insights in the details of mate-finding behavior allow predictions of the abundances of copepods in the ocean, which are useful for fisheries biologists.

National and international postgraduate lecturer Thomas Kiørboe has taught in Scandinavia, Thailand, Spain, and the United States under the auspices of EU, Nordic authorities, and DANIDA. He received his doctorate in 1988 at the University of Copenhagen. His research interests include zooplankton nutritional biology, distribution and population dynamics, small-scale biological-physical interactions, and copepod predator and prey perception. He has co-edited and been a member of the editorial board of five international journals, including the *Marine Ecology Progress Series*, *Limnology and Oceanography*, and *Journal of Plankton Research*. Dr. Kiørboe is a member of the Royal Danish Society of Science and Letters, the Danish Academy of Natural Sciences, and the Danish Council of Oceanology.

John Harte, Professor, Department of Environmental Science, Policy, and Management and Endowed Chair, Energy and Resources Group, University of California-Berkeley
Global Warming: Why the Skeptics Are Wrong
Tuesday, June 27, 2006

Professor Harte examined the current status of knowledge about global warming and review prevailing myths that surround the subject, including the notion that the uncertainties in our current models provide equal support for the concerned and the complacent. One source of uncertainty stems from the fact that most current climate models do not describe ecological responses to warming and, therefore, ignore feedback mechanisms that arise from the coupling of climate and ecosystems. He explained that climate-ecosystem feedbacks are likely to bring about future warming that is considerably more intense than is currently projected.

John Harte is an internationally known scientist on climate change and biodiversity. Recently featured on the Bill Moyers show *NOW* and in *Mother Jones* magazine, his book *Consider a Spherical Cow* is a widely used textbook on environmental modeling. Professor Harte completed undergraduate studies at Harvard and a doctoral degree from the University of Wisconsin, both in physics. He has been honored with a Pew Scholars Prize in Conservation and the Environment, a Guggenheim Fellowship, election to the California Academy of Sciences, and is the 2001 recipient of the Leo Szilard prize from the American Physical Society. He has served on six National Academy of Sciences Committees and authored more than 170 scientific publications, including six books, the latest of which, *Consider a Cylindrical Cow*, introduces the reader to a new level of environmental modeling and problem solving.

Tutorials

Tutorial on Tree Reconstruction and Coalescence Theory September 7-9, 12-13, 2005

Phylogenetic trees are commonly used to describe the evolutionary history of a group of species, and may also be used to study rapidly evolving individual organisms such as certain viruses, bacteria, or parasites. These trees are high-dimensional, non-real-valued data objects, with a specific pattern of built-in dependencies that violate the assumptions of many traditional methodologies and thus provide a rich source of statistical and mathematical challenges. This tutorial provided an introduction to the area illustrated with some interesting and important biological problems that can be addressed using phylogenetic techniques.

Tutorial on Reaction-Diffusion Models March 9-10, 2006

Reaction-Diffusion equations have been used extensively in mathematical ecology as models for the dynamics and interactions of spatially distributed populations. They provide a way of translating assumptions about local rates of movement, reproduction, and mortality into global conclusions about the persistence of populations and the structure of communities. They can be derived as continuum limits of spatially discrete stochastic processes. They can incorporate boundary conditions that describe edge-mediated effects. There are three major types of phenomena that can arise in reaction-diffusion models: traveling wavefronts, the formation of patterns in homogenous space, and the presence of lower bounds on the sizes of domains that will support non-zero solutions or solution with spatial patterns. Thus, the can be used to address issues related to biological invasions, spatial patterning, and critical patch size. The analysis of reaction-diffusion equations have monotonicity properties arising from the maximum principle which allows comparisons between solutions. The stability of their equilibria is typically determined by the signs of principal eigenvalues of related elliptic partial differential operators. Information about the stability of equilibria often can be used to analyze the overall structure of the set of equilibria or the asymptotic behavior of solutions by means of bifurcation theory and persistence theory. The derivation, interpretation, and analysis of reaction-diffusion models were discussed, along with the essential background ideas from partial differential equations and dynamical systems. Applications to biological invasions, spatial patterning, and spatial effects influencing the persistence or coexistence of populations were described.

Summer Undergraduate Program
July 5-17, 2006

The summer of 2007 marked the MBI's first summer program for undergraduates which included a two-week active survey of mathematical biology followed by a six-week Research Experience for Undergraduates (REU) program.

The first week of the program involved tutorials and hands-on computer labs in mathematical biology topics. In the first day, Dennis Pearl presented the key issues in statistical phylogenetics – aligning molecular sequences and inferring evolutionary trees from the aligned sequences. In the afternoon, Jeff Pan led the computer lab giving students a chance to try out the Clustal alignment program along with Phylip and MrBayes phylogenetics software. The second day saw David Terman leading the tutorial on the principles of mathematical neuroscience and giving participants experience with the XPP program in the afternoon computer lab. Kate Calder presented a lively tutorial on environmental statistics the following day while Hongfei Li led the afternoon computer lab using the R statistical package. The final day covered selected topics in bioinformatics presented by Ramana Davuluri, and had the students trying out some web-based bioinformatics software in the computer lab led by Greg Singer.

Dividing into teams of three or four students, the first three days of the second week gave the students a chance to study a real problem in their chosen topic area. On the following day, the students toured labs that use quantitative methods in the biological and medical sciences. This included morning tours of the labs of neuroscientist Stuart Mangel who uses the vertebrate retina as a model system for studying how the brain processes information, and the epigenetics lab of Pearlly Yan in the Center for Integrative Cancer Biology (CICB). In the afternoon, John Wenzel gave the group a tour of Ohio State's Museum of Biological Diversity with its major acarology and plant (more that a half million specimens each), insect (over 3.5 million specimens), fish (1.5 million specimens), and mollusk (150,000 specimens) collections that are available for both teaching and research. In the final tour, MBI Associate Director Libby Marschall and her team of graduate students showed off their work on the many projects in the Aquatic Ecology Laboratory. The two-week survey concluded with each of the four teams participating in a mini-conference, making both poster and oral presentations on their projects. The phylogenetics project team (Carley Matanin, Kyle Walsh, and Lisa Booth) presented an analysis of the evolution of the

bird flu virus and testing it's relation to geography, time, and host population. The mathematical neuroscience team (Ryan Chan, Adam Omidpanah, and Philip Carpenter) presented their studies of basic neurobiology and the detailed behavior of the Morris Lecar equations. Next, the environmental statistics group (Calude Davila, Nick Kefauver, Megan Meuti, and Praveen Attele) described their study of harbor seal populations in Alaska's Prince William Sound following the 1989 Exxon Valdez oil spill. The bioinformatics group presented two projects including James Sharpnack and Janet Doolittle's joint presentation on their approach to transcription factor map alignment, and Daniel Tse's CICB project on normalizing epigenetic gene expression array data. The collaborative nature of all of these efforts was illustrated as each student presented a substantial part of their group's work.

The REU component of the summer program then chose five students to spend six weeks going into much more depth in a research project in their chosen area, and closed with a second mini-conference on August 23rd where they were able to display the fruits of their efforts. Lisa Booth started the day with her analysis of the evolution of corbiculate bees. Mentored by Dennis Pearl and John Wenzel, she investigated a controversy in the evolution of honey bees, orchid bees, stingless bees, and bumble bees where behavioral and morphologic data seem to point to a different evolutionary history than molecular data. Adam Odimpanah then described his studies of REM sleep patterns under the direction of MBI Senior Associate Director David Terman. Using a three-parameter model he was able to reproduce a complex variety of key patterns of awake versus sleep versus REM sleep. Claude Davila then discussed her project guided by Kate Calder and Noel Cressie on using spatial statistical methods to investigate inorganic arsenic levels in the groundwater of Arizona. Using Kriging techniques to interpolate between measurement stations, she was able to produce estimates of both the arsenic level and the variability in this estimate across the entire state of Arizona. Next, Janet Doolittle described her studies of "support vector machine" and "random decision tree forests" techniques to investigate transcription starting points using CAGE data. Ramana Davuluri was her mentor in this bioinformatics work. Finally, Daniel Tse brought us up to date on his detailed study of normalization methods for two dye array data, sponsored by the CICB and directed by his mentor, Dustin Potter.

All of the students taking part in the MBI summer program were exposed to new areas of scholarship and appeared to gain an increased appreciation for the mathematical biosciences. The PowerPoint presentations from both the two-week and six week session mini conferences are viewable on the MBI web site.

Summer Program in Ecology and Evolution

July 17 - August 4, 2006

A total of 27 graduate students from departments of mathematics, statistics, biology, and physics, and 2 college mathematics teachers participated in the MBI's Summer Education Program on Ecology and Evolution. Of these participants, 27 came from U.S., one from Canada, and one from Chile.

The first week of the program included tutorial lectures in mathematics, statistics, and computing, as well as introductions to general biology, phylogenetics, remote sensing data, gene regulation, cancer biology, and cancer progession. Participants also spent an afternoon touring Ohio State's Olentangy River Wetland Research Park.

Kate Calder, Assistant Professor of Statistics, presented four tutorial lectures during the first week of the program. These tutorials included a general introduction to statistical modeling and inference, in addition to more special topics such as the (generalized) linear model, Bayesian hierarchical modeling, and spatial statistics. HongFei Li, a Ph.D. student in Statistics, led two computer labs which introduced the R statistical computing environment.

Yuan Lou, Associate Professor of Mathematics, presented five tutorial lectures on mathematical models from population biology, including both modeling and basic mathematical tools for analysis of these models. The topics covered were discrete-time models for population growth and selection model in population genetics, continuous-time models for both single and two species, basic tools in studying ordinary differential equations, discrete-space and continuous-time patch models, and reactions-diffusion models such as Fisher's equation (traveling wave) and logistic equation (equilibrium analysis). Three tutorials on computer simulations of these models in Matlab and XPP were given by MBI postdoctoral fellows Paul Tian, Andrew Nevai, Pranay Goel, and Partha Srinivasan.

In addition to the tutorials, several introductory lectures were given by experts in the areas of biology, genetics, and cancer related issues: Greg Singer, postdoctoral fellow at Ohio State University Medical Center (OSUMC), discussed general biology and molecular biology; Dennis Pearl, Professor of Statistics, introduced statistical phylogenetics; Tao Shi, Assistant Professor of Statistics, described the role of remote sensing data in ecological applications; Alfred Cheng, postdoctoral fellow at OSUMC, talked about epigenetic alternations in gene regulation; Michael Chang, postdoctoral fellow at OSUMC, discussed cancer biology and laboratory techniques; and Pearlly Yan, Research Assistant Professor at OSUMC, lectured on DNA methylation in cancer progression.

Following the tutorials, the project group leaders (Andrew Nevai, Partha Srinivasan, Paul Tian, Hongfei Li, Shannon LaDeau, and Dustin Potter/Pearlly Yan) introduced their projects, after which the participants are divided into six groups according to their interest. During the second two weeks of the program, the groups worked on their individual projects. On the final day of the program, each group presented their results to the entire group of participants and instructors; these presentations are available on the MBI web site.

Miniconference
Group Projects Report
August 4, 2006

Project 1: Effects of spatial heterogeneity on invasions of rare species
Project Leader: Andrew Nevai
Participants: Tucker Gilman, Katy Greenwald, Vishu Guttal, Rich Hambrock, and Will Newton

Project 2: Patterns of multiallelic polymorphism maintained by migration and selection
Project Leader: Partha Srinivasan
Participants: Anthony D'Orazio, Andre De Laire, Richard Gejji, Namyong Lee, and Ellen Peterson

Project 3: Evolution of ranges of species
Project Leader: Paul (Jianjun) Tian
Participants: Edgar Diaz, Xiaojie Hou, Etsuko Nonaka, Joaquin Rivera, and Jaffar Ali Shahul Hameed

Project 4: Spatial Modeling of Trends in Species Abundance
Project Leader: Hongfei Li
Participants: Smriti Bhotika, Ben Chan, Esprit Heestand, Manish Madan, and Hongyan Zhang

Project 5: Modeling Wild Bird Population Dynamics from Citizen Surveys
Project Leader: Shannon LaDeau
Participants: Margaret Pelosa, Aparna Sathyanarayan, Nat Seavy, Hu Wei, and Richard Yamada

Project 6: Constructing the progression pathway from normal tissue to carcinoma
Project Leader: Dustin Potter & Pearlly Yan
Participants: Flor Espinoza, Yu Liu, James Sharpnack, and Ying Wang

Seminars and Journal Clubs

Tuesday Seminar Series

Organizers: Linda Allen, Texas Tech University and Yuan Lou, The Ohio State University

Thursday Postdoctoral Seminar Series

Organizer: Sookkyung Lim, Mathematical Biosciences Institute

Sleep Seminar Series

Organizer: David Terman, Mathematical Biosciences Institute

Computational Neuroscience Journal Club

Organizer: David Terman, Mathematical Biosciences Institute

Systems Biology Journal Club

Organizer: Dustin Potter, The Ohio State University

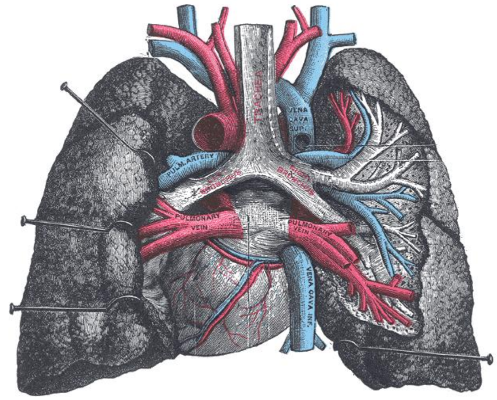
Models of Cell-Fate Journal Club

Organizer: Baltazar Aguda, Mathematical Biosciences Institute

Future Programs

Systems Physiology

September 2006 - August 2007



Much of the biological investigation of the past can be described as a compilation and categorization of the list of parts, whether as the delineation of genomic sequences, genes, proteins, or species. The past decade for example has uncovered the genetic basis for many diseases. A remaining and larger challenge is to provide an understanding of how the interactions of these biological entities across spatial and temporal scales lead to observable behavior and function. This is what systems biology is concerned with. Two important organizing principles need emphasis: (1) An integrated understanding of systems requires mathematics and the development of theory, supplemented by simulations; and (2) Theory cannot be relevant if it is not driven and inspired by experimental data. Thus the development of system biology requires collaborative work by theoreticians and experimentalists.

The goal of systems physiology is to understand how various human organs and tissues are organized and regulated to produce their normal function and pathologies. This year at the MBI will examine features of several human organ and tissue systems, including the cardiac system, the respiratory system, the microcirculatory system, the renal system, the visual processing system, the endocrine system, and the auditory system. Although these are at first glance quite different, the underlying theme is how cellular level behavior participates in the function of the whole and how feedback from the function of the whole contributes to the regulation of the cellular level behavior. Understanding of these processes may lead to new insights into the causes of diseases and how they can be treated.

Tutorials

Tutorial on the Heart: September 18-20, 2006
Organizers: Jim Keener (Department of Mathematics and Bioengineering, University of Utah), Rai Winslow (Department of Biomedical Engineering, Johns Hopkins University School of Medicine), and Andrew McCulloch (Department of Bioengineering, Whitaker Institute for Biomedical Engineering, University of California, San Diego)

Tutorial on the Lung: October 18, 2006
Organizer: Jason Bates (College of Medicine, The University of Vermont)

Tutorial for Workshop 4: January 19, 2007

Tutorial for Workshop 7: May 18, 2007

Tutorial for Workshop 8: June 22, 2007
Organizers: David Mountain (Department of Biomedical Engineering, Boston University) and James Sneyd (Department of Mathematics, University of Auckland, New Zealand)

Workshops

Cardiac Electrophysiology and Arrhythmia: September 25-29, 2006
Organizers: Jim Keener (Department of Mathematics and Bioengineering, University of Utah) and Rai Winslow (Department of Biomedical Engineering, Johns Hopkins University School of Medicine)

Cardiac Mechanics and Remodeling: October 2-6, 2006
Organizers: Jim Keener (Department of Mathematics and Bioengineering, University of Utah) and Andrew McCulloch (Department of Bioengineering, Whitaker Institute for Biomedical Engineering, University of California, San Diego)

New Approaches to Modeling Sleep/Wake Dynamics and Cognitive Performance (Sponsored by AFOSR): October 26-27, 2006
Organizers: Janet Best (Mathematical Biosciences Institute), David Terman (Mathematical Biosciences Institute), and Hans Van Dongen (Department of Psychiatry, University of Pennsylvania)

The Lung and the Respiratory (Structure, Oxygen Transport): November 6-10, 2006
Organizers: Jason Bates (College of Medicine, The University of Vermont) and Ken Lutchen (Department of Biomedical Engineering, Boston University)

Blood Flow in the Microcirculation: Function, Regulation, and Adaptation: January 22-26, 2007
Organizers: Daniel A. Beard (Department of Bioengineering, University of Washington) and Tim Secomb (Department of Physiology, The University of Arizona Health Sciences Center)

The Kidney: Cellular, Tubular, and Vascular Physiology: February 19-23, 2007
Organizers: Harold Layton (Department of Mathematics, Duke University), Leon Moore (Department of Entomology, University of Arkansas), S. Randall Thomas (Necker Faculty of Medicine), and Alan Weinstein (Department of Mathematics, University of California, Berkeley)

Workshop for Young Researchers in Mathematical Biology (WYRMB): March 12-15, 2007
Organizers: MBI Postdoctoral Fellows

Opportunities in Mathematical Biology for Under-represented Groups: March 23-25, 2007
Organizers: Carlos Castillo Chavez (Department of Mathematics, Arizona State University), Trachette Jackson (Department of Mathematics, University of Michigan), Simon Levin (Department of Ecology and Evolutionary Biology, Princeton University), and Abdul-Aziz Yakubu (Department of Mathematics, Howard University)

MicroRNA in Development and Cancer (Partially supported by the College of Medicine): April 12-13, 2007
Organizers: Carlo Croce (Department of Molecular Virology, Immunology, and Medical Genetics, The Ohio State University), George Calin (Kimmel Cancer Center, Philadelphia), Av-

ner Friedman (Mathematical Biosciences Institute), and Shili Lin (Department of Statistics, The Ohio State University)

Information Processing in the Visual System: April 23-27, 2007
Organizers: Alessandra Angelucci (John A. Moran Eye Center, University of Utah) and Paul C. Bressloff (Department of Mathematics, University of Utah)

Chemogenomics (Partially supported by the College of Medicine): May 8-10, 2007
Organizers: Paul Blower (LeadScope, Inc., Columbus, OH), Joe Verducci (Department of Statistics, The Ohio State University), John Weinstein (Genomics and Bioinformatics Group, LMP, CCR, National Cancer Institute), and Stan Young (National Institute of Statistical Sciences)

Endocrine Physiology: Type 2 Diabetes, Metabolism, and Obesity: May 21-25, 2007
Organizers: Richard Bertram (Department of Mathematics, Florida State University) and Artie Sherman (NIH-NIDDK-MRB)

Mathematics and the Undergraduate Curriculum in Biology: June 1-2, 2007
Organizers: Linda Allen (Department of Mathematics, Texas Tech University), Steve Deckelman (Department of Mathematics, Statistics, and Computer Sciences, University of Wisconsin at Madison), Jennifer Galovich (Department of Mathematics, St. John's University, Minnesota), and Libby Marschall (Department of Ecology, Evolution, and Organismal Biology, The Ohio State University)

The Auditory System: June 25-29, 2007
Organizers: David Mountain (Department of Biomedical Engineering, Boston University) and James Sneyd (Department of Mathematics, University of Auckland, New Zealand)

Bioengineering
September 2007 - August 2008

Bioengineering lies at the interfaces of biology, the applied sciences and engineering. It combines the excitement of multi-disciplinary research with the promise of making improvements to society, especially in health care, e.g. in the diagnosis and treatments of degenerative diseases. However, it is a relatively new field that is still finding its way among the established engineering and biological disciplines. As a multi-discipline it presents particular problems for the seasoned researcher as much as for the new student: indeed, we are all new students when it comes to subfields in which we have not trained.

The 2007-2008 MBI Year in Bioengineering will focus around six workshops on Metabolic Engineering, Cell and Tissue Engineering, Neuroengineering, Brain Imaging, and Neuromechanics, the latter being covered in two linked workshops. Tutorials will be offered to prepare participants, especially students and postdoctoral fellows interested in entering the field. While omitting large areas, these workshops provide examples of the central subject matter, and they highlight two key modes of operation of bioengineering: as a conduit for experimental methods, modeling and analytical tools from the physical sciences and mathematics into biology, and as a conduit for biological inspiration to the applied sciences and engineering, as in bio-inspired design of new devices and materials.

A common feature of the topics chosen, and indeed, of much of bioengineering, is their integrative nature. Biological systems are unavoidable complex, often containing many apparently redundant parts or pathways. In trying to understand, predict, control, change, or build such a complex system one must successfully reduce and combine a mass of detail. In this endeavor mathematical modeling and analysis offers a unifying language and set of principles that can draw together disparate ideas from genomics, molecular biology, neuroscience, biochemistry, physiology, imaging and signal processing (to name only topics germane to the six MBI workshops). Mathematics can also reveal common principles operating on different time and space scales, and guide the development of computational algorithms for simulation and data analysis.

Tutorials

Tutorial for Workshop 2: October 18-19, 2007

Tutorial for Workshop 3, Introductory orientation on comparative biomechanics of locomotion I: January 10-11, 2008

Tutorial for Workshop 4, Introductory orientation on comparative biomechanics of locomotion II: March 27-28, 2008

Tutorial for Workshop 5, Brain physiology related to movement control and epilepsy: May 8-9, 2008

Tutorial for Workshop 6

Workshops

Metabolic Engineering: September 24-28, 2007
Organizers: John Doyle (Department of Electrical Engineering, California Institute of Technology), David Gang (Department of Plant Sciences, University of Arizona), and Michael Savageau (Department of Biomedical Engineering, University of California, Davis)

Cell and Tissue Engineering: October 22-26, 2007
Organizer: Melissa L. Knothe Tate (Lerner Research Institute, Department of Biomedical Engineering, The Cleveland Clinic) and Stanislav Shvartsman (Department of Chemical Engineering, Princeton University)

Microfluids: November 12-14, 2007
Organizer: Andre Levchenko (The Whitaker Institute for Biomedical Engineering, Johns Hopkins University)

Biomechanics - Muscle and Whole Body: January 14-18, 2008
Organizers: Art Kuo (Department of Mechanical Engineering, Department of Biomedical Engineering, Institute of Gerontology, University of Michigan) and Lena Ting (Laboratory for Neuroengineering, Georgia Tech)

Neuromechanics of Locomotion: March 31 - April 4, 2008
Organizers: Ansgar Bueschges (Biology Department, University of Cologne), Robert J. Full (IBIBI-Integrative Biology, University of California, Berkeley), and Philip J. Holmes (Department of Mechanical and Aerospace Engineering, Princeton University)

Restoration of Movement Via Peripheral Nerve Stimulation: April

Real Time Brain Interfacing Applications: May 12-15, 2008
Organizers: Dawn Taylor (Department of Biomedical Engineering, Case Western Reserve University) and David Terman (Mathematical Biosciences Institute)

Brain Imaging: June 9-13, 2008
Organizers: Sylvain Bouix (Psychiatry Neuroimaging Laboratory, Brigham and Women's Hospital), Kaleem Siddiqi (Centre for Intelligent Machines, School of Computer Science, McGill University), Stefano Soatto (Department of Computer Science, University of California, Los Angeles), Allen Tannenbaum (School of Electrical and Computer Engineering, Georgia Institute of Technology)

Systems Biology of Decision Making: June 16-20, 2008
Organizers: Nigel Franks (Department of Biological Sciences, University of Bristol), Naomi Leonard (Department of Mechanical and Aerospace Engineering, Princeton University), Kevin Passino (Department of Electrical and Computer Engineering, Control Research Laboratory, The Ohio State University), Roger Ratcliff (Department of Psychology, The Ohio State University), Thomas Seeley (Department of Neurobiology & Behavior, Cornell University), and Thomas Waite (Department of Evolution, Ecology, and Organismal Biology)

Jennings Hall Renovation

The Jennings Hall project will be completed on May 1, 2007. The MBI will move into its new location at Jennings Hall in the summer of 2007.

Jennings Hall is located in the heart of the College of Biological Sciences, less than five minutes' walk from the OSU Medical School, and within eight minutes' walk of the College of Mathematical and Physical Sciences as well as the Mathematics and Statistics Departments.

Upon moving into Jennings Hall, the MBI will have a newly renovated 9,100 square feet (as compared to its current 5,100 square feet), including an auditorium equipped with state of the art Access Grid videoconferencing technology.

Publications

Technical Report No. 43
Authors: Avner Friedman and Gheorghe Craciun
Title: Approximate traveling waves in linear reaction-hyperbolic equations
Date of Publication: September 2005

Technical Report No. 44
Authors: Julie A. Besco, Robert Hooft van Huijsduijnen, Adrienne Frostholm, and Andrej Rotter
Title: Receptor protein tyrosine photophatase rho interacts with components of adherens junctions
Date of Publication: November 2005

Technical Report No. 45
Authors: Robert Stephen Cantrell, Chris Cosner, and Yuan Lou
Title: Advection-mediated coexistence of competing species
Date of Publication: January 2006

Technical Report No. 46
Authors: Yuan Lou, Salome Martinez, and Peter Polacik
Title: Loops and branches of coexistence states in a Lotka-Volterra competition model
Date of Publication: January 2006

Technical Report No. 47
Authors: Zailong Wang, Pearlly Yan, Dustin Potter, Chris Eng, Tim H. Huang, and Shili Lin
Title: Heritable clustering algorithms for recapturing epigenetic progression in breast cancer
Date of Publication: February 2006

Technical Report No. 48
Authors: Zailong Wang and Shili Lin
Title: Modeling and analysis of SAGE libraries
Date of Publication: February 2006

Technical Report No. 49
Authors: Sharmila Venugopal, Joseph B. Travers, and David H. Terman
Title: A computational model for motor pattern switching between taste-induced ingestion and rejection oromotor behaviors
Date of Publication: February 2006

Technical Report No. 50
Authors: Gheorghe Craciun, Yangzhong Tang, and Martin Feinberg
Title: Understanding bistability in complex enzyme-driven reaction networks
Date of Publication: March 2006

Technical Report No. 51
Authors: Ji Zhou, Shili Lin, Vince Melfi, and Joe Verducci
Title: Composite MicroRNA target predictions and comparisons of several prediction algorithms
Date of Publication: April 2006

Technical Report No. 52
Author: Winfried Just
Title: Reverse engineering discrete dynamical systems from data sets with random input vectors
Date of Publication: April 2006

Technical Report No. 53
Authors: Liang Liu and Dennis K. Pearl
Title: Species trees from gene trees: Reconstructing Bayesian posterior distributions of a species phylogeny using estimated gene tree distributions
Date of Publication: June 2006

Technical Report No. 54
Authors: Guangyu Sui, Meng Fan, Irakli Loladze, and Yang Kuang
Title: The dynamics of a stoichiometric plant-herbivore model and its discrete analog
Date of Publication: June 2006

Technical Report No. 55
Authors: Ishwar V. Basawa, U. Narayan Bhat, and Jin Zhou
Title: Parameter estimation in queuing systems using partial information
Date of Publication: June 2006

MBI Volumes on Tutorials in Mathematical Biosciences
Published by Springer-Verlag
Volume I: Mathematical Neuroscience (2004)
Volume II: Mathematical Modeling of Calcium Dynamics and Signal Transduction (2005)
Volume III: Cell Cycle, Proliferation, and Cancer (2006)

MBI Newsletter
Fall 2005, Volume I, Issue 1
Winter 2006, Volume I, Issue 2
Spring 2006, Volume I, Issue 3