International Clinics on Infectious Disease Dynamics and Data

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Project Summary

Mathematics and simulation are essential tools in infectious disease control, enabling decision-makers to explore control policies before implementing them, interpret trends, and predict emerging threats. This project draws on our years of experience organizing and running courses on infectious disease dynamics in South Africa and builds on the foundation laid by earlier Clinics by promoting repeated interaction with the most promising students as they develop in their research careers. The proposed program comprises 2 distinct but overlapping International Clinics on Infectious Disease Dynamics and Data and a complementary research scholars exchange program.

The **Clinic on the Meaningful Modeling of Epidemiological Data (MMED)**, to be held annually in South Africa, targets quantitative scientists, including mathematicians, statisticians, computer scientists, and selected infectious disease epidemiologists. Participants engage with meaningful questions about infectious disease dynamics by integrating mathematical models with epidemiological data.

The **Clinic on Dynamic Approaches to Infectious Disease Data (DAIDD)**, to be held annually at the University of Florida, targets public health researchers and population biologists interested in studying infectious diseases. Instruction will focus on how the complex dynamics of pathogen transmission influence study design and data collection for addressing problems in infectious disease research.

The **International Disease Dynamics and Data Research Scholars Exchange Program (I3D)** will allow selected Clinic participants to engage further with Clinic faculty. The program will fund scholars to spend 6 weeks working on an approved research project at the faculty member's home institution. I3D scholars from Africa will work with faculty at North American institutions, and American I3D scholars will work with faculty at African institutions. The I3D scholars program will complement the two annual clinics to provide a near-continuous flow of collaborative research between the two continents.

The proposed project will directly support over 150 junior investigators from the US and Africa and indirectly support an additional 150-200 African researchers through their participation in the MMED clinics, which will be directly supported by the South African Centre for Epidemiological Modelling and Analysis (SACEMA) and the African Institute for Mathematical Sciences (AIMS).

Narrative

Many important current problems in infectious disease control and prevention – such as the potential for test-and-treat programs to curtail HIV/AIDS transmission and the development of strategies for trachoma elimination – are best understood through a combination of mathematical models of infectious disease dynamics, well-designed field trials, and careful analysis of observational and experimental data. The International Clinics on Infectious Disease Dynamics and Data (ICI3D) program will provide a unique and much needed opportunity for junior researchers from the US and Africa to develop the toolsets necessary to conduct this type of research and to communicate their questions, methods, and findings across interdisciplinary boundaries.

Specific Aims of the Proposed ICI3D Program

Specific Aim 1: *To build international capacity in data-driven modeling of infectious disease dynamics for addressing important public health problems.*

Many countries in the developing world face serious burdens from infectious disease, but lack specific expertise in mathematical and statistical techniques for studying infectious disease dynamics. The MMED clinic targets Africans who have the technical foundation, but not the broad expertise, to tackle these problems, providing the necessary toolsets to engage with both public health data and public health practitioners in a meaningful way. The new DAIDD clinic will teach African epidemiologists and population biologists principles of dynamical thinking relevant to study design and necessary for communication with infectious disease modelers. The I3D research exchange program will allow African researchers to spend time in a research lab at a North American institution and to complete a research project with a Clinic faculty member, further strengthening their ties to the international infectious disease dynamics research community.

Specific Aim 2: *To provide junior US-based researchers with meaningful international experience working in interdisciplinary research teams.*

International training opportunities of this type are essential for young American scientists, as the up-and-coming generation of researchers will be tasked to grapple with increasingly global problems that require engagement across both disciplinary and geographic boundaries. The MMED clinic provides junior researchers an opportunity to participate in the program in South Africa and encourages development of group projects with African collaborators. The DAIDD clinic will provide a forum for interaction with international researchers. The I3D Research Scholars Exchange Program will provide funds for American MMED and DAIDD graduates to complete a research project with African collaborators.

Specific Aim 3: *To develop and maintain a collaborative international network of infectious disease researchers with complementary toolsets and a common vocabulary.*

Together, the MMED clinic, DAIDD clinic, and I3D program will create a near continuous intercontinental flow of ideas and researchers engaging with infectious disease dynamics and data. To aid collaboration in the interstices, and maintain the engagement of program participants not involved in the I3D program, we will provide an online collaboration environment open to all program participants in the form of a Working Wiki. This forum will allow researchers to maintain collaborations developed at the Clinics and stimulate the development of new collaborations.

Specific Aim 4: *To create open access resources for training in data-driven modeling of infectious disease dynamics.*

Lecture slides, tutorials, and other training materials from the MMED and DAIDD clinics will be made available via open access licensing. Many materials from MMED 2010 and MMED 2011 are already available for free download on the MMED website (http://lalashan.mcmaster.ca/theobio/mmed). In the first year of the proposed project, all computer tutorials will be compiled into a package for the R statistical computing language. Materials will be updated as needed, and we will actively seek new ways to disseminate these materials to a broad audience of infectious disease researchers. The Working Wiki collaboration environment and appropriate documentation will also be made available to researchers who would like to use this format for collaborations outside the ICI3D program.

Research Education Program Plan

Acronyms used in the Research Education Program Plan

AIC	Akaike's Information Criterion
AIDS	Acquired Immunodeficiency Syndrome
AIMS	African Institute for Mathematical Sciences
ASI	Advanced Study Institute
CEPH	Council on Education of Public Health
CIDA	Canadian International Development Agency
CITI	Collaborative Institutional Training Initiative
DAIDD	Clinic on Dynamical Approaches to Infectious Disease Data
DIMACS	Center for Discrete Mathematics and Applied Computer Science (Rutgers University)
EPI	Emerging Pathogens Institute
HIV	Human Immunodeficiency Virus
I3D	International Disease Dynamics and Data Research Scholars Exchange Program
ICI3D	International Clinics on Infectious Disease Dynamics and Data
IRB	Institutional Review Board
MBI	Mathematical Biosciences Institute (Ohio State University)
MIDAS	Models of Infectious Disease Agent Study
MMBD	Clinic on the Meaningful Modeling of Biological Data (2009)
MMED	Clinic on the Meaningful Modeling of Epidemiological Data
MMF	Muizenberg Mathematical Fever
NIH	US National Institutes of Health
NSF	US National Science Foundation
ODE	Ordinary Differential Equation
PDE	Partial Differential Equation
PEPFAR	President's Emergency Plan for AIDS Relief
PI	Principal Investigator
RFA	Request for Applications
RAPIDD	Research and Policy for Infectious Disease Dynamics Program
SACEMA	South African Centre for Epidemiological Modelling and Analysis
SIR	Susceptible-Infectious-Removed (family of models)
TB	Tuberculosis
UCSF	University of California, San Francisco
UF	University of Florida
US	United States
WHO	World Health Organization

Sections in the Research Education Program Plan

A	Program Directors
B	Program Faculty/Staff
C	Proposed Research Education Plan
D	Training in the Responsible Conduct of Research
E	Program Participants
F	Diversity Recruitment and Retention Plan
G	Evaluation and Tracking
H	Preliminary Work

A Program Directors

Juliet Pulliam, PhD – Dr. Pulliam is an Assistant Professor in the Department of Biology and Emerging Pathogens Institute (EPI) at the University of Florida (UF). Prior to joining the faculty at UF, she was a Research and Policy for Infectious Disease Dynamics (RAPIDD) Program Fellow in the Division of International Epidemiology and Population Studies at the Fogarty International Center, NIH. She earned a doctoral degree in Ecology and Evolutionary Biology from Princeton University in 2007 and worked as a postdoctoral fellow at the Center for Disease Ecology at Emory University. Dr. Pulliam's research focuses on quantitative approaches to understanding the determinants and dynamics of viral host jumps, with a particular focus on the epidemiology and ecology of zoonotic encephalitis viruses and viral zoonoses of livestock. Her work on these topics has been published in high-profile journals including *Science*, *Nature Reviews Microbiology*, and *Journal of Infectious Diseases*. She has been a leading force in the development of, and an instructor in, the Clinic on the Meaningful Modeling of Epidemiological Data and its precursor programs since 2008. As the Principal Investigator, she will be responsible for the expansion of the MMED collaboration into the full ICI3D program and will oversee all aspects of programmatic development.

Alex Welte, PhD – Dr. Welte, as Director of the South African Centre for Epidemiological Modelling and Analysis (SACEMA), has contributed significantly to the MMED program. As the Consortium PI for SACEMA in the ICI3D program, Dr. Welte will continue to play a key role in the training, and also in the recruitment of African applicants to the program and the sustaining of the emerging collaborative network for infectious disease modeling in Africa. A physicist by training, Dr. Welte has a distinguished track record in the field of infectious disease modeling, in particular for HIV. Since SACEMA's inception, Dr. Welte has been central to curricular development and delivery of SACEMA's epidemiological modeling short courses. He has advised the local authorities in South Africa, the international normative bodies and major funding agencies on methodological developments in HIV modeling and surveillance, with a focus on capacity development. At SACEMA, he presently coordinates a major "modeling for policy" project funded by the Canadian International Development Agency (CIDA), and collaborates with the South African national centers of excellence in HIV/AIDS and TB, as well as the key regional field based research groups linked to the Desmond Tutu Foundation.

B Program Faculty/Staff

B.1 Core Program Faculty

Jonathan Dushoff, PhD – Dr. Dushoff is an associate professor at McMaster University in Hamilton, Canada. He has a broad research program in computational and mathematical approaches to studying the evolution and spread of infectious diseases of humans, with a strong statistical component. Particular research interests include interactions between beliefs, behaviors and disease spread, and canine rabies in Africa and Asia. He has taught short courses annually in South Africa since 2007 and has been instrumental in building and maintaining the MMED program.

John Hargrove, PhD – Dr. Hargrove is a Professor of Mathematical Sciences at Stellenbosch University and was the first director of SACEMA. For more than 40 years, he has combined fieldwork and mathematical epidemiology to understand the population

dynamics and control of tsetse flies, the vectors of Human African Trypanosomiasis. Since 1999 Dr. Hargrove shifted focus more towards the analysis and modeling of data in the world of HIV. As the director of SACEMA, he spearheaded efforts in capacity building for epidemiological modeling in Africa, and he has been a key player in the development of the MMED clinic and its precursor programs since 2006.

Travis Porco, MPH, PhD – Dr. Porco is an Associate Professor in the Department of Epidemiology and Biostatistics and the Department of Ophthalmology at the University of California, San Francisco (UCSF). Prior to joining the faculty at UCSF, he was Senior Epidemiologist in the Surveillance and Epidemiology Section of the California state Tuberculosis Control Branch. His doctoral degree is in Biophysics from the University of California, Berkeley. Dr. Porco's research focuses on agent-based simulation of contact investigation as a means for disease control, and applying mathematical models of disease transmission to clinical trials for controlling trachoma (with T. Lietman). He has been an instructor in the Meaningful Modeling of Epidemiological Data clinic and its precursor programs since 2008, and also collaborated with A. Galvani in developing a modeling workshop for public health and nursing students held at the University of KwaZulu-Natal in 2009. Dr. Porco has taught an introduction to mathematical epidemiology at the University of California, Berkeley, School of Public Health since 2006.

James Scott, MPH, PhD – Dr. Scott is an Assistant Professor of Statistics in the Department of Mathematics and Statistics at Colby College. He completed his graduate studies at the University of California, Berkeley earning a doctorate in Epidemiology and master's degrees in both Biostatistics and Public Health. He has worked as a computer programmer, an epidemiologist for the State of California, and has taught numerous courses in both epidemiology and statistics. His research has focused on transmission of infectious diseases including HIV, tuberculosis, and water-borne pathogens. He has been involved with the planning and execution of the MMED clinics for the past three years.

Brian Williams, PhD – Dr. Brian Williams has recently retired from the TB program in the World Health Organization (WHO). Having originally studied Physics, first at the University of Natal and then at Cambridge University, he has carried out research in solid-state physics, ecology and epidemiology. Before joining the WHO in 2001 he was the Director of the Epidemiological Research Unit in Johannesburg where he led research into occupational diseases of mine-workers, especially TB and silicosis. In 1994, as the epidemic of HIV/AIDS became apparent in South Africa, he set up the Mothusimpilo Project in Carletonville, South Africa, the biggest gold-mining complex in the world. There he worked with mine-workers, sex-workers and adolescents to understand and to find ways to manage the epidemic of HV. Most recently he has been closely involved with developing and promoting the use of treatment-as-prevention to stop the epidemic of HIV. He conceived the idea of a center for the application of mathematics to biological systems in South Africa which led to the founding of SACEMA and has recently been appointed to the scientific advisory board of PEPFAR, the President's Emergency Plan for AIDS Relief. Dr. Williams has contributed to the MMED clinics and precursor programs since 2009, inspiring participants to tackle the challenge of learning to do meaningful modeling that will have real-world public health impacts.

Steve Bellan, MPH – Mr. Bellan is a PhD candidate at the University of California, Berkeley. His research focuses on developing statistical and mathematical models in

parallel with empirical studies to gain insight into infectious disease dynamics and control in both humans and animals. He is particularly interested in spatial aspects of epidemiological problems and is currently working on integrating multiple data sets from a range of spatiotemporal scales to estimate the burden of anthrax in the plains herbivores of Etosha National Park, Namibia. Mr. Bellan was a participant in the Advanced Study Institute on Mathematical Epidemiology held in 2007 and 2008. He was asked to join the faculty of the Clinic on the Meaningful Modeling of Biological Data in 2009 and has been a key player in the development of the MMED clinics. Mr. Bellan expects to complete his doctoral work prior to the grant's start date (July 1, 2012), and in addition to contributing to instruction for the ICI3D program, he will be responsible for development, distribution, and maintenance of the ICI3D R package and other open access instructional materials.

B.2 Additional Program Faculty

Wim Delva, MD, PhD – Dr. Delva is a medical doctor and epidemiologist with a joint research appointment at the International Centre for Reproductive Health at Ghent University in Belgium and SACEMA. In late 2006, Dr. Delva organized a conference entitled "Bridging the gap between modeling and reality: the added value of interdisciplinary collaboration in the fight against TB and HIV," which was an important pre-cursor to MMED initiative. Dr. Delva gave guest lectures at the Clinics in 2010 and 2011, and he is expected to be among the African faculty to attend the DAIDD clinics held at UF. He currently supervises several former MMED participants and may participate in the I3D program as a research mentor.

B.3 Program Staff

Gavin Hitchcock, PhD – Dr. Hitchcock is Assistant Director for Training at SACEMA, where he is responsible for all training workshops conducted by SACEMA and for the overall training and supervision of all SACEMA funded students throughout South Africa. Dr. Hitchcock is a mathematician and educator with long experience in University teaching and academic program design and management in Southern Africa. He was the recipient of a Distinguished Teacher Award from the University of Zimbabwe in 2001. Dr. Hitchcock evaluated the MMBD clinic in 2009 and the MMED clinics in 2010 and 2011. In this program, he will conduct the evaluation of the MMED clinics, the DAIDD pilot and clinics, and the I3D program. He will also coordinate the selection of African candidates for the MMED clinics and will contribute to local logistical arrangements.

Lee Worden, PhD – Dr. Worden is an applied mathematician by training and is also an experienced software developer. He is the author and maintainer of WorkingWiki, a freely-available software extension for the popular MediaWiki platform that transforms a standard wiki into a powerful environment for collaboration on data analysis processes, simulation programs, and publication-quality manuscripts. He will continue to develop and maintain the WorkingWiki extension, tailoring it to the needs of ICI3D program participants.

C Proposed Research Education Program

C.1 Significance

Despite tremendous advances over the course of the past century, infectious diseases remain an important source of morbidity and mortality worldwide. In 2008, infectious diseases accounted for 68% of the global mortality burden in children under 5 [1]. These deaths are concentrated primarily in low-to-middle income countries; in Africa, the estimated percentage of under-5 deaths due to infectious causes is close to 80% [1]. Developing countries also suffer the greatest overall burden from major infectious diseases such as HIV/AIDS, TB, and malaria [2-5]. For example, of 33.3 million adults and children estimated to be living with HIV/AIDS worldwide in 2009, over two-thirds reside in sub-Saharan Africa [2]. However, these countries have the least scientific research capacity to address infectious diseases and other global public health problems [6].

Integration of dynamic models and data is an increasingly important feature of public health research and decision-making. For example, data-driven modeling has recently played an important role in spurring serious consideration of test-and-treat programs for HIV/AIDS patients and male circumcision as important tools for eliminating HIV transmission [7-11]. Dynamic models also play an important role in the design and analysis of clinical trials for a variety of infectious disease, such as those aimed at identifying effective tools for the elimination of trachoma, the world's leading infectious cause of blindness [12-22], and those aimed at assessing the safety and efficacy of vaccines in development for dengue fever [23].

Few programs exist that explicitly train junior investigators to link models and data for addressing applied problems – particularly in the areas of the world most affected by high infectious disease burdens. Our Clinic on the Meaningful Modeling of Epidemiological Data (MMED) and its precursor programs, which have run annually since 2006, have been the first serious attempt to address this gap in Africa [24]. To date, the Clinics have had a remarkable impact on participants in the program. For example, of 12 undergraduates who attended the program in 2009-2010, none of whom had experience in quantitative epidemiology prior to the Clinic, 5 are now pursuing Masters degrees in the field through programs linked with SACEMA or AIMS. The program also provides valuable international experience for young American researchers, giving them a head start for engaging in an increasingly global scientific research community.

C.2 Innovation

This proposal outlines our vision for expanding the MMED collaboration from a single annual clinic into a year-round collaborative research network, sustained by 2 annual clinics, a research scholars exchange program, and the development and maintenance of a collaborative online research community. The proposed International Clinics on Infectious Disease Dynamics and Data (ICI3D) program will simultaneously build African capacity for data-driven infectious disease modeling and create strong links between African and American infectious disease researchers.

The ICI3D program will make innovative use of technology for teaching, for example by simulcasting selected Clinic sessions to program participants unable to attend in person and by working with a software developer to tailor his software for online technical collaborations to the program's needs. We will continue to develop innovative pedagogical tools for interdisciplinary education, such as the Muizenberg Mathematical Fever exercise described below, which was specifically designed to meet the needs of MMED participants. Furthermore, we will update and expand the instructional materials we make available via open access licensing and will provide further documentation of these materials to facilitate their use in other contexts.

C.3 Approach

The ICI3D program is structured to provide maximum interaction between American and African researchers from the full spectrum of research disciplines engaged with population-level processes that affect infectious disease dynamics – including mathematicians, statisticians, computer scientists, disease ecologists, sociologists, demographers, and medical, veterinary, and public health epidemiologists. This will be done by conducting two complementary workshops each year – the Clinic on the Meaningful Modeling of Epidemiological Data (MMED), which has been run since 2010 and targets primarily quantitative scientists, and the new Clinic on Dynamical Approaches to Infectious Disease Data (DAIDD), which will teach modeling principles and aspects of study design for dynamic systems to researchers with little or no background in mathematical modeling (Figure 1). Based on our experience with MMED and its precursor programs, we expect that a small number of MMED participants will be sufficiently oriented toward data collection to benefit from also attending the DAIDD clinic; likewise, we expect that a small number of DAIDD participants will have sufficiently sophisticated quantitative skills to participate in the MMED clinic. We will encourage such cross-fertilization as appropriate. In addition, the International Disease Dynamics and Data (I3D) Research Scholars Exchange Program will foster close interaction with the most promising MMED and DAIDD graduates, ensuring they have the support they need for further development of their research careers and providing a mechanism for allowing them to complete research publications in collaboration with Clinic faculty.

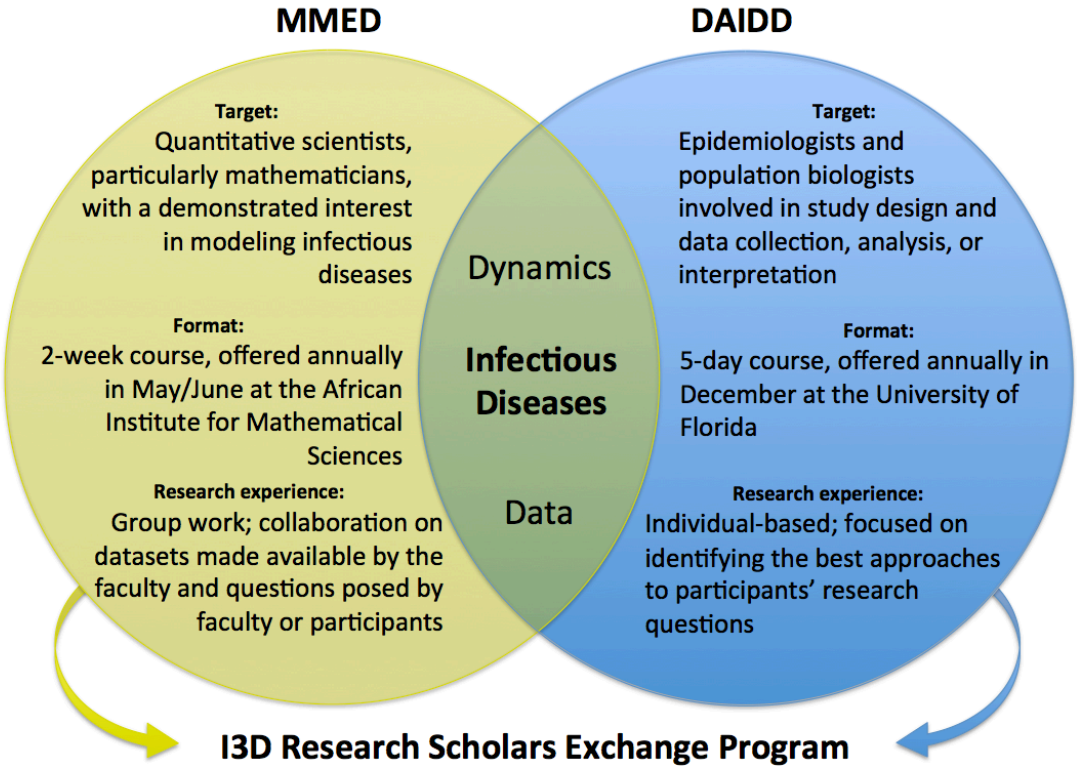

Figure 1: International Clinics on Infectious Disease Dynamics and Data (ICI3D) program structure

C.3.1 Clinic on the Meaningful Modeling of Epidemiological Data (MMED)

MMED arose from the observation that many mathematicians are highly motivated to apply their modeling skills to public health problems, but require further training to bridge the gap between theory and real-world applications. The primary focus of these clinics is to illustrate techniques for integrating mathematical models with data, moving gradually from hands-on classroom exercises to independent exploration of novel research ideas. An overview of the 2-week program is given in Figure 2.

Building meaningful models requires understanding how to ask meaningful questions. Thus, several clinic sessions are devoted to asking participants to simply look at real public health data from diseases such as HIV/AIDS, tuberculosis, trachoma, and measles. Participants then describe what they see, and discuss potential drivers of observed patterns. This helps participants notice patterns in the data, and consider interpreting these patterns in the light of epidemiological knowledge and data limitations. Once a meaningful question is formed, a model can become a tool for formulating and testing hypotheses. We teach participants to use data to inform the construction of the simplest or clearest models appropriate to answer a given question, rather than focusing on the development of complex mathematical models unrelated to data.

The original target of the MMED and predecessor programs was African post-graduate students in biomathematics, and these still constitute the core of the program. We have come to believe, however, that diversity enhances the collective learning experience. Thus clinic participants come from a wide range of backgrounds, from epidemiologists to statisticians to mathematicians, and from advanced undergraduates all the way to established faculty. African participants are supported directly by our partner institutions, AIMS and SACEMA; this proposal covers costs for American participants and US-based Clinic faculty, including travel, room and board.

While we recognize that mathematical approaches provide a rich, rigorous framework in which to answer complex questions, we also believe that for effective research and collaboration, mathematical epidemiologists must recognize the expertise necessary and complexities involved in the development and execution of empirical studies in epidemiology. To that end, we balance clinic sessions on mathematical material with sessions on study design, data analysis, and logistics. The first week of the program is devoted mainly to lectures and computer tutorials, and the second week focuses heavily on research projects. Key components of the MMED program are described below.

Interactive lectures

The first week of the MMED clinic, and to a lesser extent the second week, includes a series of interactive lectures designed to give participants the background and tools they need to begin engaging in data-driven modeling. For the most part, these lectures are presented in a casual manner intended to encourage discussion and critical, independent thinking about the concepts being presented. The interactive lectures that form the core of the MMED program and will be repeated in future Clinics cover the following topics:

- Introduction to Thinking about Data (Williams, Scott)
- Public Health, Epidemiology, and Models (Scott)
- History of Mathematical Disease Modeling (Porco)
- Introduction to Infectious Disease Data (Pulliam)
- Why fit models to data? (Welte)
- Variability, Sampling Distributions, and Simulations (Scott)

- Thinking about Antenatal Clinic Data as a Measure of HIV Prevalence (Hargrove)
- Distributed Delay Models of Survival (Bellan)
- Study Design and Analysis in Epidemiology (Bellan, Porco)
- Introduction to Data Management and Cleaning (Pulliam)
- Introduction to Statistical Philosophy (Dushoff)
- Introduction to Likelihood (Bellan)
- Likelihood Fitting and Dynamic Models (Bellan, Dushoff)
- Doing Science (Williams)
- Test-and-treat Programs for HIV Elimination (Williams)
- Demographic Stochasticity (Dushoff)
- Introduction to Model Assessment (Pulliam)

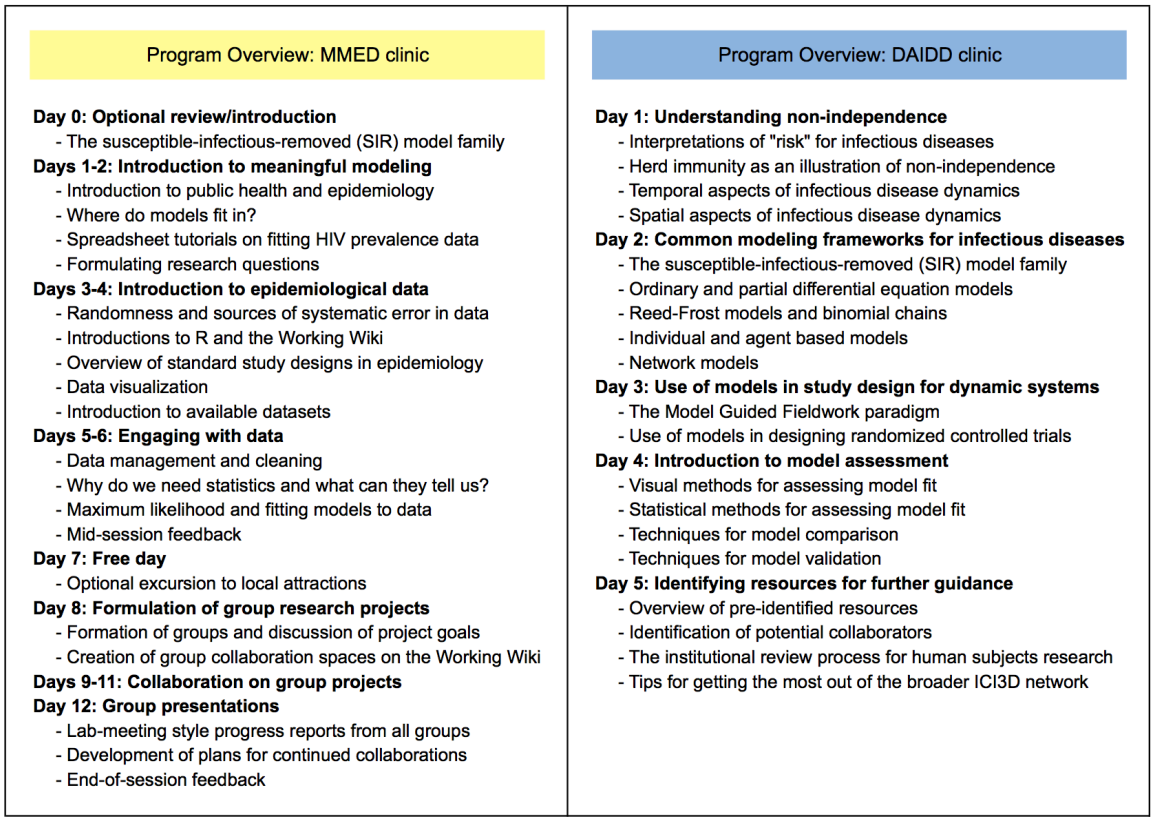

Figure 2: Overview of the programs for the Clinic on the Meaningful Modeling of Epidemiological Data (MMED) and the Clinic on Dynamical Approaches to Infectious Disease Data

Faculty research talks

To give participants a broader perspective on how data and models can be combined to address specific public health questions, Clinic faculty give evening talks on their own recent research projects. In 2011, faculty gave research talks on the following topics:

- Modeling the spread and control of canine rabies in East Africa (Dushoff)
- Using models to inform public health control strategies: water, sanitation, and hygiene (Scott)

- Nipah virus in Bangladesh: approaches integrating models and data (Pulliam)
- Anthrax incidence estimation in wildlife using distance sampling and scavenger movement data (Bellan)
- Childhood mortality reductions from mass administration of azithromycin: lessons from a community randomized trial in Ethiopia (Porco)

Poster sessions

Poster sessions provide an opportunity for all MMED participants to present on their own research. Several weeks prior to the workshop, participants are provided with information to help them design a well-structured poster. Beginning in 2012, participants will be asked to send an electronic version of the poster to SACEMA several days before the Clinic, and all posters will be printed at SACEMA. This will ensure that all participants have access to a large-format printer and will give participants a professional memento that can be hung at their home institutions upon their return. Three one-hour poster sessions will be held during the first few days of the Clinic, and the posters will be displayed for the full 2 weeks to ensure that all faculty and participants have an opportunity to view each poster.

Reading groups

Participants are asked to read 3 papers before or during the Clinic, as an introduction to the literature in the field of data-driven infectious disease modeling. Two of these papers are discussed in small, pre-assigned groups consisting of 4-6 participants and 1 faculty member. These two papers are selected as a pair, presenting a classic view of a topic and a modern take on the same topic. In 2011, these papers focused on seasonality of measles dynamics. We first discussed a paper published by Bartlett in 1957 that included statistical analysis and simulation of measles outbreaks in England and Wales [25]; we later discussed a paper by Ferrari *et al*. from 2010 that used more modern techniques – and considerably more powerful computational resources – to examine seasonal forcing of measles transmission in Niger [26]. By pairing the readings in this way, participants gained some insight into how the field has evolved and how current work builds on earlier studies.

The third paper, which is discussed by the full group, is selected to illustrate how models can be used to drive public health policy. These discussions are led by Brian Williams. In 2010 and 2011, the papers focused on the potential of test-and-treat programs (or "treatment as prevention") to impact the course of the HIV epidemic and TB incidence in sub-Saharan Africa [8, 27]. By providing examples of the impact models can have when they are designed to address meaningful questions, these sessions are key for motivating participants to step outside the traditions of their own disciplines and learn the techniques required to do meaningful data-driven modeling.

Formulating and communicating research questions

In this exercise, we ask participants to go through a series of steps designed to help them think about their approach to research and about communicating their research to those outside their specialization. At the conclusion of the exercise, participants are asked to post their modified research questions to their profile on the Working Wiki. The full exercise is described on the MMED clinic website: http://lalashan.mcmaster.ca/theobio/mmed/index.php/Thinking_about_research_questions

Mentors program

The mentors program was developed in 2011 as a first step in the eventual recruitment of Africans who have been trained in the program to the Clinic faculty, which we view as an essential goal for program sustainability and a central hallmark of successful capacity development. This program provides an opportunity for several of the most promising past African MMED participants – those with both strong research potential and a demonstrated ability to communicate effectively – to engage with the Clinic's material and faculty on a deeper level. These individuals are invited to return to MMED as "mentors" and have specified responsibilities to carry out both prior to and during the Clinic.

Working Wiki

The MMED clinc relies on wikis both for long-distance advanced planning, and for organizing and exchanging information during the Clinics. We have an *organizer* wiki for planning, development and exchanging ideas; a *public* wiki (i.e., the MMED website: http://lalashan.mcmaster.ca/theobio/mmed) for sharing information with prospective participants and other interested parties, and to make course materials publicly available; and a *participant* wiki, which we use to share information and data, and collaborate during the workshops and beyond. The participant wiki is referred to throughout the proposal as "the Working Wiki." Participants in the MMED clinic have indefinite access to the Working Wiki. This wiki houses a wide variety of material, including research profiles for each participant; pages describing the progress and plans of the research project groups; pages with links to resources on mathematics, statistics and public health; links to various data sources (including some shared with participants by special permission); and information about local culture and social events of interest to participants.

This participant wiki makes use of WorkingWiki, a MediaWiki extension we are developing to allow wikis to host reproducible research [28, 29]. WorkingWiki allows us, for example, to develop, debug, and run R scripts collaboratively, while maintaining a history of the development; or to edit and view LaTeX documents which directly incorporate figures and tables generated on the wiki by our scripts. WorkingWiki also provides a platform on which research can be shared with the community in a form that is friendly and accessible, while also being very easy to implement and modify. WorkingWiki projects can be downloaded *in toto* and run on a reader's machine; the reader can then experiment with modifications to the published analysis or simulations. More information on the WorkingWiki extension is available on the WorkingWiki project website: http://lalashan.mcmaster.ca/theobio/projects/index.php/WorkingWiki

Computer tutorials

During the Clinic, participants work through a series of computer tutorials designed to illustrate different aspects of the scientific process and of integrating models with data. In order to allow students to begin manipulating dynamic models and fitting them to data on the first day of the Clinic, the initial tutorials involve fitting spreadsheet-based models of HIV transmission to prevalence data (in the Open Office program Calc). On the second day, participants are introduced to the statistical programming language R, which provides more powerful and flexible computing options. We ask participants to work through a series of introductory R tutorials during days 2 and 3 of the workshop:

- Tutorial 1: Introduction to R and Its Quirks

- Tutorial 2: More on Vectors, Data Frames, and Functions
- Tutorial 3: Probability Distributions and Control Structures

From day 3 on, each lecture is paired with a complementary R tutorial, which students can work through on their own, and additional tutorials are made available on certain advanced topics. Substantial time is devoted to computer sessions throughout the 2-week program; however, it is not expected that all participants will complete each tutorial during the course of the Clinic. Rather, they are asked to work through those tutorials they feel will be most useful for their own work and interests, and they are reminded that they can work through any remaining tutorials upon return to their home institutions. The following R tutorials are currently available:

- Visualizing Infectious Disease Data in R
- Data Management and Cleaning in R
- Simulations, Probability, and Sampling Distributions
- Using Maximum Likelihood to Estimate an Infectious Period Distribution
- Introduction to Stochastic Susceptible-Infectious-Recovered (SIR) models
- Introduction to Fitting Dynamic Models
- Multidimensional Parameter Optimization for Fitting Dynamic Models
- Odds ratios and Logistic Regression
- Generalized Linear Models and Multimodel Selection and Inference using AIC

Additional tutorials will be developed for use in future MMED and DAIDD clinic. Topics for future tutorials are likely to include Network Construction and Visualization, Simulation of Infection Dynamics on Networks, Timeseries Methods for Infectious Disease Data, and Introduction to Spatial Statistics.

One-on-one mentoring sessions

Throughout the 2 weeks of the Clinic, timeslots are made available for participants to sign up for one-on-one meetings with Clinic faculty. These meetings can be used to address any topic that the participant finds useful, such as feedback on their own research projects, guidance on career development, or assistance with technical material.

Muizenberg Mathematical Fever (MMF)

During MMED 2010 we developed a pedagogical exercise known as Muizenberg Mathematical Fever (MMF) that bridges the traditional distinction between mathematical and biomedical epidemiology and has become a cornerstone of the MMED program. The exercise consists of a real-time simulation of a stochastic outbreak in course participants, where the “infectious agent” is a piece of paper. Index cases are initiated through surreptitious distribution of a small number of infection forms on the first day of the Clinic. The paper provides simple instructions for newly infected individuals. Following the instructions, infected individuals use a Poisson random number generator in R to determine the number of potentially infectious contacts they will generate. They then print out that many new infection forms from a webpage, discreetly hand these to other participants (without knowledge of who has already been infected), and record the time of these “infectious contacts.” A Bernoulli random number generator is similarly used to determine whether or not their infection is symptomatic, and only symptomatic individuals report to our “health care system” (a specified faculty member) that they are sick. All new infections, however, are reported to a second faculty member via email.

"Recovery" consists of delivering the infecting paper to a third faculty member. Thus, each outbreak generates two data sets: (1) a realistic provider-based surveillance system that records symptomatic cases and time of symptom onset, and (2) an unrealistically accurate knowledge of the underlying transmission dynamics.

MMF produces "outbreaks" that percolate through participants before burning out – much like epidemics of biological pathogens. While we predetermine aspects of the natural history of infection (such as the basic reproduction number and the symptomatic proportion), participants' behavior (i.e. whom they infect and how quickly) also affects disease dynamics, and the unpredictable nature of these events adds to the realism of the outbreak. During the 2011 outbreak, we dictated that those who had attended MMED 2010 (primarily Clinic faculty) would be immune to MMF, thereby seeding a protective factor for participants to discover during the analytical stage of the exercise. The data from the outbreaks give participants the opportunity to apply a variety of methods from both risk factor epidemiology and mathematical epidemiology to characterize and understand the transmission process, and we place an emphasis on understanding all the steps from data collection to analysis. Table 1 describes some of the MMF-based research projects that groups of participants have carried out. Conducting these projects has helped reveal to participants each method's assumptions and utilities, clarifying how the various risk factor and mathematical methods differ from and complement each other. We are in the process of publishing a paper that describes the MMF exercise in sufficient detail for it to be adopted as a pedagogical tool in other contexts [30].

Table 1: Projects based on the Muizenberg Mathematical Fever exercise

Field	Study	Analysis	Data	Goal	Pedagogical value
Risk factor	Case-control or cohort	Logistic or Poisson regression (generalized linear model)	Disease outcomes and risk factors	Understand what variables increase (or decrease) risk of disease/infection	Exposure to survey design, data entry and cleaning, and statistical methods; understand effects of confounding and bias in data analysis
Mathematical	Estimation of R_0 and infectious period	Probability distribution fit to infectious contact data and infectious periods	Contact-tracing data and observed infectious periods	Characterize individual heterogeneity in infectiousness and overall pathogen contagiousness	Understand utility of contact tracing data in characterizing disease dynamics; understand R_0 as epidemic threshold; understand how individual variation can affect disease dynamics
	Outbreak simulation	Stochastic SIR - individual-based using Gillespie algorithm	Estimates of R_0, incubation and infectious periods	Understand how outbreak size is affected by immune proportion	Awareness of effects of stochasticity in outbreaks of small sizes; development of intuition for how simulation can be used to answer applied questions

Group research projects

In the second week of the Clinic, much of the schedule is devoted to development of working groups focused on active research questions. The questions addressed can be posed by Clinic faculty or by participants, and each group consists of 4-6 participants with different backgrounds, paired with 1-2 Clinic faculty and mentors. Most working groups focus on integrating models with data made available on the Working Wiki. In 2010 and 2011, questions addressed by these working groups included:

- *Can trachoma be eliminated by only treating children from 1 to 10 years of age?* This group used trachoma data from a clinical trial in Ethiopia to help formulate a model that takes into account age-related differences in transmission and susceptibility.
- *Can HIV incidence rates be inferred from age-structured prevalence data?* This group used data from antenatal clinic studies in Zimbabwe to develop a model for extracting incidence estimates.
- *Is HIV transmission in couples more likely to result from transmission between partners or from extra-partnership infection?* This group used data on seroconcordance and serodiscordance to examine the relative importance of HIV transmission from within and outside long-term partnerships. Using a probability model to estimate the frequency of different types of transmission, they compared transmission patterns in couples from populations across Africa.

Several project groups have also formed around data collection and analysis from the Clinic's MMF outbreaks. Participants in these working groups gain experience with questionnaire design, data collection, entry, and management, and outbreak investigation. In 2011, one group conducted a retrospective cohort study of Clinic participants and successfully identified attendance at MMED 2010 as a protective factor against MMF infection, in the process learning concepts of confounding and bias; another group investigated the impact of social networks on MMF spread.

Group research reports

In 2012, we will introduce the requirement that, in addition to oral progress reports on the final day of the Clinic, project groups will produce a written report on their work to be submitted via the participant wiki by August 31. At this time, groups will be asked to indicate whether they intend to pursue peer-reviewed publication of the project. If so, they will receive detailed feedback on the report (including an assessment of whether the goal of publishing the work is realistic). Pending approval from the Clinic faculty, reports on projects that will not be pursued for peer-reviewed publication (including, for example, any projects based on MMF data) will be posted online under an open access license and available via the MMED, ICI3D, and/or SACEMA websites.

Beginning with MMED 2012 graduates, only those participants whose groups have submitted a suitable report will be eligible for selection as an I3D research scholar. Nominated individuals will be notified of this requirement when invited to submit an I3D proposal.

C.3.2 Clinic on Dynamic Approaches to Infectious Disease Data (DAIDD)

The DAIDD clinics will incorporate aspects of the MMED program (such as the exercise on formulating and communicating research questions) but will target public health researchers and population biologists with a good grounding in classical (frequentist)

statistics and experience with data collection but little or no knowledge of dynamical systems theory or infectious disease modeling. The detailed program will be developed through weekly conference calls among North American faculty, with regular input from African faculty. This model was used successfully to develop the MMED program. The overall structure for the 5-day program is outlined in Figure 2, and certain features of the proposed program are highlighted below.

Guest lectures

In addition to lectures on core material from the Clinic faculty, participants will benefit from the broad base of expertise in quantitative approaches to infectious disease dynamics that comes with holding the Clinic on UF's main campus and from EPI's institutional support. Each day of the Clinic will feature a 1-hour guest lecture from an invited speaker. These guest lectures will be timed to allow simulcasting to the broader ICI3D program network, including those based at SACEMA with whom we will set up 2-way communications to allow long-distance participation in the question-and-answer periods following each lecture. We anticipate that different individuals will give the guest lectures each year. Potential speakers include the following EPI faculty:

- Dr. Dana Focks, Research Professor of Environmental and Global Health
- Dr. Jed Keesling, Professor and Chair of Mathematics
- Dr. Ira Longini, Professor of Biostatistics
- Dr. Rick Rheingans, Associate Professor of Environmental and Global Health
- Dr. Burton Singer, Courtesy Professor, National Academy of Sciences member
- Dr. Andy Tatem, Assistant Professor of Geography

Individual research plans

One of the main goals of the DAIDD clinics is to give participants the tools to incorporate appropriate dynamical approaches into their own research plans. Given the short format of these Clinics, we do not expect participants to complete a research project in the timeframe of the Clinic; rather we will ask them to use the Clinic as an opportunity to develop a research plan, which can then be used as a framework for grant or dissertation proposals when they return to their home institutions. Working closely with their peers and with Clinic faculty, each participant will develop a research plan that contains the following elements

- Statement of the key research questions
- Identification of appropriate quantitative tools for addressing the research questions, including specific modeling frameworks
- Justification of the choice of tools, based on a discussion of their assumptions, advantages, and limitations
- Discussion of how quantitative approaches will be used in both study design and data analysis
- For research involving human subjects, discussion of potential concerns and identification of the appropriate Institutional Review Board for protocol submission
- Identification of additional resources that will be used in the study design and data analysis phases of the proposed project (e.g., relevant papers and texts)
- Identification of potential collaborators at the home institution and/or in the ICI3D program network

Only those participants who submit a suitable written research plan will be eligible for selection as an I3D research scholar.

C.3.3 International Disease Dynamics and Data (I3D) Research Scholars Exchange Program

The I3D research scholars exchange program will allow the most promising researchers among MMED and DAIDD graduates to spend 6 weeks completing a research project with a member of the ICI3D faculty. Potential scholars can be nominated by any of the Clinic faculty, and nominated participants will be invited to submit a project proposal (see the section on selection of participants for further details).

During the 6-week exchange program, visiting research scholars will be fully integrated into the lab group of the supervising faculty member and will carry out a research plan tailored to the scholar's background and the proposed project. Figure 3 shows an example research plan for a hypothetical I3D scholar. All I3D scholars will be expected to give an oral or written report on their work at the end of the 6-week project period and will be required to submit a final written report after returning to their home institution. In most cases, the final written report is expected to be in the form of a manuscript formatted for submission to a journal agreed upon by the scholar and the supervising faculty member. I3D scholars will also be encouraged to give conference presentations on their work.

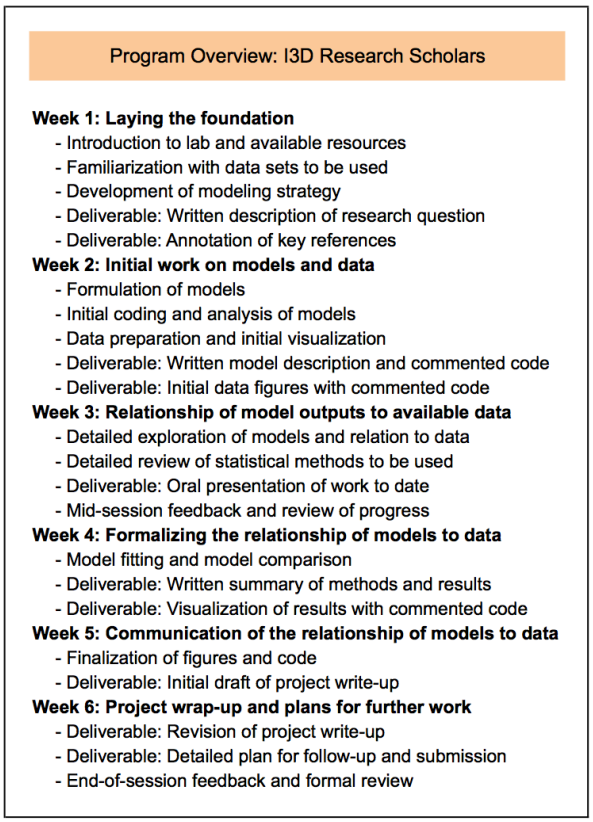

Figure 3: Example research plan for a hypothetical International Disease Dynamics and Data (I3D) Research Exchange Scholar

D Training in Responsible Conduct of Research

Formal training in the responsible conduct of research involving human subjects will be offered during the DAIDD clinics and recorded or simulcast for viewing by other ICI3D program participants. This formal training will offer an introductory overview to issues of confidentiality and informed consent, and will give a generic description of the institutional review process for research involving human subjects. DAIDD participants are expected to attend all Clinic sessions, including this training. For DAIDD participants who plan to collect or analyze individual-level data, the written research plan must include identification of the appropriate IRB at the participant's home institution for protocol submission.

Applied, informal training in the ethical conduct of clinical trials is included in sessions on study design for randomized controlled trials, given by Dr. Porco. These sessions focus on clinical trials aimed at identifying methods for trachoma elimination and involve discussion of issues from the ethics of randomization to the need for intermediate evaluation and determination of stopping criteria. Dr. Porco has covered these topics at MMED and its precursor programs since 2008, and will present similar material at the DAIDD clinics.

Further informal training on the responsible conduct of research is provided at MMED through the discussion of data sets shared with participants. Several of the datasets used are shared with participants by special permission, and the conditions of use – including what permissions are needed before publishing on the data – are discussed with participants and posted on the wiki pages where data are made available. A further opportunity for informal instruction is provided by the MMF exercise, and participants collecting data on MMF spread are asked to consider issues of confidentiality and to deidentify the datasets they construct before they begin analysis.

All I3D research scholars will be required to complete online training in conducting international human subjects research through the CITI International Training Platform, prior to beginning the research exchange. Although I3D scholars are not expected to collect human subjects data, we believe it is essential that they be aware of ethical and procedural issues surrounding the collection and use of such data. The CITI International Training Platform, unlike other CITI training programs, is publicly available and thus provides a platform for uniform instruction for I3D scholars, independent of whether their home and host institutions are institutional users of the CITI program. More information on this program is available through the CITI website (https://www.citiprogram.org). Additional guidance for I3D scholars on the responsible conduct of research, including discussion of responsible authorship and data sharing, will be provided as needed on an informal basis.

Finally, the participant wiki gives us an additional forum for providing resources on the responsible conduct of research, and we will create a page on this topic with links to information about authorship criteria, conflicts of interest, proper documentation of sources, and data sharing and management, as well as to the CITI International Training Platform. This page will be linked from the main page of the wiki, and both faculty and participants will be able to share new resources that they find particularly useful or relevant with the full ICI3D research community.

E Program Participants

E.1 Recruitment of participants

Figure 4 outlines the annual recruitment schedule for the three program components.

E.1.1 Recruitment for MMED clinics

In 2011, we solicited applications by sending a request for applications (RFA) to contacts in mathematics departments, ecology programs, and public health schools. We also posted the RFA on the MMED website and asked former participants to circulate the RFA at their home institutions. We received complete applications from 19 applicants at institutions based in the US (13) and Canada (6), including graduate students, post-baccalaureate students, and post-doctoral researchers. We accepted 8 of these applicants and had to decline an equal number of qualified candidates (see description of selection criteria below).

To recruit for future MMED clinics, we will expand the distribution of the RFA to take full advantage of the professional networks of Clinic faculty, including the Research and Policy for Infectious Disease Dynamics (RAPIDD) Program and the Models of Infectious Disease Agent Study (MIDAS). We will also distribute the RFA to institutions and campus groups that will help target women, under-represented minorities, and persons with disabilities, as described in the diversity recruitment and retention plan.

E.1.2 Recruitment for DAIDD clinics

DAIDD participants from US institutions will be recruited in a similar manner to that described above for MMED, with an additional emphasis on distribution of the RFA to all US schools of public health accredited by the Council on Education of Public Health (CEPH).

Solicitation of applications for DAIDD participants from Africa will utilize the professional networks of African faculty and former participants. In addition, North American Clinic faculty will ask contacts who work on infectious diseases in Africa to distribute the RFA to their local colleagues. We will also take advantage of existing networks, such as the Afrique One Initiative and the African Field Epidemiology Network, to disseminate the RFA outside our own professional networks.

E.1.3 Recruitment for I3D program

The I3D program is in large part a response to calls from former participants for opportunities to engage with Clinic faculty after the MMED clinic. As such, the I3D program will have a closed application process, with applications accepted by invitation only (see description of the selection process for further details).

Month	MMED Recruitment Schedule	DAIDD Recruitment Schedule	I3D Recruitment Schedule	Month
Dec	MMED RFA			Dec
Jan			I3D Nomination and Invitation	Jan
Feb	**Application deadline: Feb 1**			Feb
Mar	Admission notifications: Mar 1		**Application deadline: Mar 1**	Mar
Apr	Waitlist closed: Apr 15		Selection notifications: Apr 1	Apr
May				May
Jun				Jun
Jul		DAIDD RFA	I3D Nomination and Invitation	Jul
Aug				Aug
Sep		**Application deadline: Sept 1**	**Application deadline: Sept 1**	Sep
Oct		Admission notifications: Oct 1	Selection notifications: Oct 1	Oct
Nov		Waitlist closed: Nov 1		Nov

Figure 4: ICI3D Program annual recruitment schedule (Cycle: December - November).

E.2 Selection of participants

E.2.1 Selection of participants for MMED clinics

MMED participants are selected from an open application process. All MMED applicants must submit the following materials:

- Electronic application form (required)
- A current *curriculum vitae* (required)
- An abstract of no more than 400 words describing a current or former research project to be presented at the Clinic (required)
- A statement of interest and intent indicating how the experience would enhance their short-term and long-term research goals (required)
- If applicable, a letter requesting travel support and the amount of funding that will be required.
- A letter of recommendation (required for post-graduate and graduate students only, to be submitted separately by the faculty member writing the recommendation).

North American Clinic faculty (Pulliam, Dushoff, Porco, Bellan, and Scott) are responsible for reviewing US-based applicants. At least 2 faculty members (assigned randomly after recusal for potential conflicts of interest) conduct an initial review of each application. The initial reviews require reading the entire application and providing 2 scores based on the application materials, the "essentials score" and the “desired score.” The “essentials score” indicates whether the applicant has the background that is required for them to be selected, which may be demonstrated through coursework, publications, or earlier degrees. Each of the following areas is assigned 1 point:

- dynamics (eg, ODEs, PDEs, or nonlinear systems)
- probability and/or classical statistics
- biological thinking
- computational proficiency

The “desired score” indicates whether the applicant has other qualities that are strongly desired, each worth 1 or 2 points:

- potential to bring something new to the table (a perspective that wouldn't otherwise be represented) and/or clear evidence of creative, independent thinking (2 points)
- a strong desire to attend (1 point)
- a high likelihood of benefiting from the Clinic (2 points)

The “essentials score” varies from 0 to 4, and applicants with an average score below 3 are omitted from further consideration. The remaining applicants are given an initial ranking based on their average “desired score,” and their full applications are read by all North American Clinic faculty. The initial ranking is used as a starting point for discussion of the applicants and debate regarding admissions decisions. A final ranking is reached by consensus, and qualified candidates who are not initially admitted are placed on a ranked waiting list in case higher-ranked applicants are unable to attend.

Selection of African MMED participants is conducted by Drs. Welte, Hargrove, and Hitchcock. The process for selecting these participants, supported through funds from SACEMA, is similar.

MMED mentors are selected by the faculty from among African participants in earlier MMED clinics. The mentors are selected on the basis of their demonstrated technical skills, their ability to clearly communicate complex information, their level of engagement with the material, and their willingness to help those who are struggling. Participants are monitored throughout the Clinic to determine their suitability as future mentors, and at the end of the Clinic, faculty nominate and discuss potential mentors until a consensus is reached on which nominees are most suitable.

E.2.2 Selection of participants for DAIDD clinics

The application and selection process for the DAIDD pilot and clinics will be similar to that described above for MMED; however, the "essentials score" will be tailored to the target audience, with 1 point each assigned for appropriate background or experience in classical statistics (e.g., hypothesis testing and sample size calculations), data collection and/or management, basic infectious disease concepts, and differential and integral calculus.

In addition, evidence of support for the applicant to pursue their proposed research plan upon return to the home institution (e.g., as indicated in the reference letter from a faculty advisor) will be taken into account when considering the likelihood that the participant will benefit from the Clinic. The participant selection process will be adjusted as necessary following the DAIDD pilot in 2012.

E.2.3 Selection of participants for I3D Research Scholars Exchange Program

All participants in the MMED and DAIDD clinics, including participants in MMED 2010 and 2011, will be eligible for nomination by ICI3D faculty to participate in the I3D scholars program. Nominated participants will be invited to prepare a research proposal in collaboration with a faculty supervisor and submit an application for consideration. The proposed supervisor is chosen by the nominee and may or may not be the nominating faculty member. African participants must choose a faculty supervisor based at a North American institution, and American participants must choose a faculty supervisor based at an African institution. The completed application should include the following elements:

- a 2-page description of the proposed research project
- a 6-week research plan for the exchange period
- a budget proposal, which should include travel, room and board costs and may include specified scholarly expenses (up to $6,000 total expenses)
- a paragraph describing the reasons for selecting the proposed faculty supervisor
- a letter (or verbal communication) from the proposed ICI3D faculty member in support of the application
- a letter from the nominee's supervisor at his or her home institution, indicating support for participation in the program and continuation of the project following the 6-week exchange

Because applicants will be preselected through the nomination process, the primary factor determining the selection of I3D research scholars from among the nominees will be a reasonable expectation that the proposed project will lead to a research publication. For nominees who are undergraduate, post-graduate, or Masters students, a conference presentation may be a more suitable goal and would be the expectation. In addition to the application materials, the extent of communication with the proposed supervisor

during proposal preparation and completion of written requirements from the MMED and DAIDD clinics will be considered in scholar selection.

F Diversity recruitment and retention plan

We have a strong record of recruiting diverse participants from both African and North American institutions. Table 2 shows Clinic participants from each continent for 2009-2011, stratified by sex and race. Of the 92 participants since 2009, 38 have been women (8 of 17 from North American institutions) and 68 have been non-white (7 of 17 from North American institutions). We are firmly committed to maintaining, and further expanding, the diversity of program participants, through both recruitment and retention efforts.

F.1 Diversity recruitment

We will recruit diversity, including participation of women, under-represented minorities, individuals from low-income backgrounds (particularly among African participants), and persons with disabilities, primarily by striving to attract a diverse applicant pool and by selecting participants representative of this diversity. We will work with University of Florida's Division of Student Affairs, including the Disability Resource Office and the Multicultural and Diversity Affairs group, to ensure that information about the program and all RFA's are distributed to a wide diversity of students, both on and – through the professional networks of their staff – outside the UF community. In addition, we will consider the other resources available to participants when making funding allocation decisions for American MMED participants, opting to give full support to those who are least likely to be able to secure funding from other sources. We expect that this will enhance our ability to successfully recruit a diverse set of participants.

Table 2: Clinic participants, by sex and race (2009-2011)

Participants based at African Institutions*	2009	2010	2011	Total**
Total	**20**	**32**	**38**	**75**
By sex				
Male	13	19	21	**45**
Female	7	13	17	**30**
By race				
Black	16	23	24	**51**
White	3	4	6	**14**
Other	1	5	8	**10**
Participants based at North American Institutions	2009	2010	2011	Total
Total	**4**	**5**	**8**	**17**
By sex				
Male	2	3	4	**9**
Female	3	1	4	**8**
By race				
Black	1	1	3	**5**
White	3	3	4	**10**
Other	1		1	**2**

* These participants have been supported through SACEMA and AIMS.

** Totals in this column may not equal the sum of 2009-2011 columns due to single inclusion of repeat participants.

F.2 Diversity retention

At past MMED clinics, we have worked very hard to integrate students across cultural, racial, and disciplinary boundaries. We do this primarily by providing opportunities for participants to socialize with each other and with faculty but also by requiring that, for certain exercises early in the Clinic, participants form groups or work with partners whom they had not met prior to the Clinic. We believe that our success in creating a sense of community among our diverse participants is one of the key factors motivating participants to return to the Clinic (e.g. through the mentors program) and will play an important role in attracting participation in the I3D research scholars exchange program. We will ensure that participants selected as mentors and nominated as I3D candidates represent the full diversity of the MMED and DAIDD clinics, and we will guarantee that selected individuals' financial situations do not prevent them from participating in these more selective programs by providing full financial support to mentors and I3D scholars for the duration of these programs.

G Evaluation and Tracking Plan

G.1 Evaluation of program components

G.1.1 Evaluation of the MMED clinics

Evaluation of the MMED clinics will be conducted each year by Dr. Gavin Hitchcock (SACEMA), as has been done for previous Clinics. Dr. Hitchcock runs two feedback sessions during each Clinic; these sessions are closed to the Clinic faculty. At the end of the first week, the feedback session focuses mainly on how well the Clinic is meeting participants' needs in order to identify potential modifications that can be made to the schedule for the second week. Dr. Hitchcock provides a written summary of the main points from this session to the Clinic faculty in time for any necessary modifications to be incorporated into the second week of the program. At the end of the Clinic, Dr. Hitchcock runs a second session that solicits verbal feedback on all aspects of the Clinic, from instruction to group work to accommodation. Participants are also asked to complete a short, anonymous written evaluation that asks a series of questions regarding suggested improvements and includes scoring the overall satisfaction with each of the following items on a five-point scale (from low to excellent):

- the value of the Clinic
- lectures by faculty
- research talks from faculty
- research talks from mentors
- one-on-one mentoring sessions
- reading groups
- student presentations (oral and poster)
- R tutorials
- spreadsheet exercises on fitting models to data
- group projects
- social activities
- use of the Working Wiki
- experience provided in modeling real-life data

All of the feedback from the on-site sessions and written evaluations is summarized into an annual report on the Clinic, which is made available to all Clinic faculty. The report on MMED 2011 is included as an appendix to this proposal. The suggestions for modifications and scores for different aspects of the program are actively considered in the development of the program for each following Clinic. We believe that continued evaluation along these lines will be essential for meeting the changing needs of Clinic participants as the infectious disease dynamics and data research community grows.

G.1.2 Evaluation of the DAIDD pilot and clinics

Overall, the DAIDD clinics will be evaluated in a similar manner to the MMED clinics, though the evaluation of the DAIDD pilot will include additional evaluation components to ensure that the full program is designed to meet participants' needs. Dr. Hitchcock will assess all aspects of the pilot program based on his personal observations, verbal interviews with all participants during the course of the Clinic, the formal feedback session, and retrospective evaluation by participants in response to an email questionnaire. These various modes of evaluation were used to assess the MMBD clinic in 2009, and Dr. Hitchcock's resulting report was extremely useful to the Clinic faculty in developing the full MMED program for 2010.

G.1.3 Evaluation of the I3D program

Evaluation of the I3D program will include assessment of the program structure, the guidance provided by the supervising faculty member, the scholar's progress at the end of the 6-week exchange, and the quality of the final written report. Because this aspect of the program is will be dispersed in time and space, Dr. Hitchcock will coordinate the evaluation by email, soliciting written feedback from both the scholar and the supervising faculty member. As with the MMED clinics, structured feedback will be sought mid-session to allow adjustments to the research plan or to interactions between the scholar and supervisor. Feedback from both parties will also be solicited at the end of the exchange. In addition, external feedback will be sought on the scholar's progress at this time. For scholars giving oral presentations at the end of the exchange, the external assessment will be solicited either from a local expert at the hosting institution or from an ICI3D faculty member who attends the presentation virtually. Similarly, for scholars submitting a written report at the end of the 6-week exchange, the report will be read by at least one ICI3D faculty member or external expert other than the supervising faculty member. These evaluations will focus on identifying concrete steps to be completed before a manuscript can be submitted to a journal for peer review. The supervising faculty member will also comment on the final written report and either indicate that the manuscript is ready for submission or provide additional feedback, briefly outlining further work to be done.

G.2 Tracking of Participants

All ICI3D program participants will be tracked via an annual Internet survey for at least 5 years from their most recent formal participation in the program (i.e., attendance at a Clinic or participation in the I3D scholarship exchange). Participants will be asked to indicate the year/s and program/s they attended and to updated their title, affiliation, degrees in progress, and preferred email address. They will then be asked to answer a series of questions regarding the impact of the program on their current work and on their career plans. They will be asked to list any publications influenced by the program

and indicate the publication's status (in preparation, submitted, or published). Unlike the written end-of-session evaluations conducted by Dr. Hitchcock for each of the Clinics, these surveys will not be anonymous; however, participants will be asked whether they give permission for their responses to be quoted (e.g., in promotional materials) and whether or not their responses should be attributed to them.

G.3 Program outcomes and benchmarks

Beyond the annual evaluation of the program based on participants' feedback, the overall success of the program will be assessed by the impact it has on participants' career trajectories. This will be assessed through a combination of retrospective feedback from participants gathered via the tracking questionnaire and observed outcomes tracked by other means, such as ICI3D program records or the standard tracking conducted for SACEMA funded students. Benchmarks of success to be assessed include the following:

- percentage of accepted applicants who attend each Clinic (target: 95%)
- percentage of MMED research groups completing written research reports (target: 90%)
- percentage of DAIDD participants completing written research plan (target: 100%)
- percentage of MMED research groups that publish papers from research conducted (target: 10%)
- percentage of invited MMED mentors who accept and attend (target: 90%)
- percentage of invited I3D nominees submitting a complete proposal (target: 80%)
- percentage of I3D scholars who publish papers from research conducted (target: 70%)
- percentage of I3D scholars who publish papers from or give conference presentations on research conducted (target: 90%)
- percentage of undergraduates attending the MMED clinic who pursue Masters degrees related to infectious disease dynamics and data (target: 50%)
- percentage of Masters students attending the MMED clinic who pursue PhD's related to infectious disease dynamics and data or public health (target: 50%)
- percentage of PhD students attending the MMED Clinic who pursue postdoctoral positions related to infectious disease dynamics and data or careers related to public health (target: 70%)
- percentage of graduate students attending the DAIDD clinic who complete a thesis or dissertation with a dynamical component (target: 70%)
- percentage of participants in the DAIDD clinic who pursue funding for a research project with a dynamical component to study design and/or data analysis (target: 70%)
- percentage of participants in the DAIDD clinic who successfully attain funding for a research project with a dynamical component to study design and/or data analysis (target: 50%)
- percentage of publications resulting from the ICI3D program that have authors from US and African institutions (target: 80%)
- percentage of publications resulting from the ICI3D program that have at least one participant (i.e., non-faculty) as an author (target: 90%)
- number of publications resulting from the ICI3D program with at least one participant as author (target: 12)

- recruitment of new Clinic faculty from among African participants (target: at least 1)
- percentage of program participants responding to the annual internet survey (target: 60%)
- increasingly positive feedback on the written end-of-session evaluations for each aspect of the program (e.g., increasing proportion of marks indicating “very good” or “excellent” for each aspect)

We believe the targets indicated next to each benchmark are ambitious but attainable.

H Preliminary Work

H.1 Advanced Study Institute (ASI) in Mathematical Epidemiology

The current MMED clinics grew out of the DIMACS/MBI US-Africa Biomathematics Initiative, funded by NSF, and built on the foundation initially laid by the DIMACS workshop on “Facing the challenges of Infectious Diseases in Africa,” in September 2006. Three faculty members in the current proposal (Hargrove, Welte, and Delva) were centrally involved in this first workshop, specifically designed to bring together African-American and African epidemiologists. The workshop pointed to the need for the training of Africans in epidemiological modeling and led naturally to the Advanced Study Institute (ASI) in Mathematical Epidemiology held at the African Institute for Mathematical Sciences (AIMS) in 2007 and 2008. Whereas the ASI provided African and American students an overview of, and introduction to, the mathematical theory of epidemics, MMED provides training in how to link mathematical models to data. Several of the ICI3D faculty were involved in the ASI as instructors (Dushoff, Hargrove in 2007; Dushoff, Hargrove, Pulliam, and Porco in 2008) or participants (Bellan in 2007 and 2008). The 2007 ASI was primarily lecture-based, providing participants with background information. The 2008 ASI brought back a selected subset of the participants from 2007 to allow group work on infectious disease modeling projects.

H.2 Clinic on the Meaningful Modeling of Biological Data (MMBD)

The Clinic on the Meaningful Modeling of Biological Data (MMBD), held at AIMS in 2009, was developed in response to the largely theoretical focus of the ASI and the unmet need for training African infectious disease modelers to engage meaningfully with data. The MMBD clinic was a 1-week program supported by DIMACS, AIMS, and SACEMA. Participants were also invited to stay for an additional 3 days of unstructured time to develop research projects, individually or in groups. The clinic focused largely on exploring the integration of models with timeseries data on HIV prevalence at antenatal clinics across Africa and timeseries data on TB incidence in African countries. Through interactive lectures and computer tutorials, students constructed simple models with a variety of underlying assumptions and discussed why these models succeeded or failed to reproduce patterns observed in the data. Participants also discussed differences in observed patterns across the continent and possible mechanisms to explain these differences. The schedule for MMBD 2009 can be viewed online (http://users.aims.ac.za/~juliet/mmbd/schedule.php).

In many ways MMBD was a pilot for what became the MMED clinic. Most of the MMED faculty were involved in its development and execution (Hargrove, Dushoff,

Pulliam, Porco, Bellan, Scott, and Williams), and many of the topics covered and materials used have been updated and incorporated in later years.

H.3 Clinic on the Meaningful Modeling of Epidemiological Data (MMED)

H.3.1 MMED 2010

In 2010, we expanded the Clinic to a 2-week format in order to allow a richer program that provided both greater breadth and greater depth of exposure to topics in infectious disease dynamics and data. The program was expanded to include faculty research lectures, one-on-one mentoring sessions, the Muizenberg Mathematical Fever exercise, additional R tutorials, lectures on fitting dynamic models to data using maximum likelihood, material on standard epidemiologic study design and analysis, and development of group projects. Reading groups were introduced, with participants asked to read 5 papers, and all participants gave a short oral research presentation. This two-week format has worked well and is the basic structure proposed for future MMED clinics. MMED 2010 was supported by funds from DIMACS, SACEMA, and AIMS. The schedule for the 2010 Clinic is available online, linked from the main MMED website (http://lalashan.mcmaster.ca/theobio/mmed).

H.3.2 MMED 2011

In 2011, we added an additional focus on communicating research across disciplinary boundaries and introduced the mentor program. We also responded to feedback from MMED 2010 that indicated participants were worn out by the end of the first week by reducing the number of reading groups from 5 to 3 and introducing a poster session to replace some participant talks. The response to the poster session was so enthusiastic that we have decided to hold multiple poster sessions at MMED 2012 *in lieu* of participant research talks. The schedule for MMED 2011 is also linked from the main MMED website.

MMED 2011 was supported by the Ecology of Infectious Diseases Program of the US National Science Foundation and the UCSF/Berkeley Framework for Global Health Program, funded by the US National Institutes of Health's Fogarty International Center. One of the stated goals of the DIMACS/MBI US-Africa Biomathematics Initiative was to inspire the development of spin-off programs, and the MMED clinics are the first such program to become fully independent.

In addition, the various editions of Clinics have created capacity ripe for other programs, such as the TB Symposium planned for 2012 by a consortium comprising the University of Pittsburgh's Graduate School of Public Health, SACEMA, and the Centre for Infectious Diseases at Stellenbosch University. Several of the ICI3D faculty will also serve as consortium or external faculty for that program if it is funded.

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Facilities and other resources

Institutional Commitment

The ICI3D program has very strong support from the Consortium institutions and other institutional partners. This support is detailed in the description of consortium and contractual agreements and in letters provided by appropriate officials at each of these institutions:

- Dr. Alex Welte, co-PI on this grant and Director of SACEMA
- Prof. Barry W. Green, Director of AIMS
- Keith Herndon, Associate Director and Administrator of the Emerging Pathogens Institute at the University of Florida
- Lori Kletzer, Vice President for Academic Affairs and Dean of Faculty at Colby College

Visa arrangements for all intercontinental travel requiring visa processing will be handled by the University of Florida International Center (UFIC), under the guidance of Dr. Sandra Russo, Director of Program Development and Federal Relations at UFIC. Visa processing for MMED participants traveling within Africa will be handled through SACEMA and AIMS, as has been done for previous iterations of the MMED clinic. Program venues and resources available for each of the ICI3D program components are described below.

Program venue for MMED clinics

The MMED clinics are held at the African Institute for Mathematical Sciences (AIMS) in Muizenberg, Cape Town, South Africa. Muizenberg is a surfer's haven nestled between beach and mountains on the beautiful Cape Peninsula. The MMED clinics and precursor programs have been held at AIMS annually since 2006. For these meetings, AIMS has provided lecture space, computer access and support, office space for faculty, and various forms of logistical support. In 2012, AIMS will open new facilities that are specifically designed for use by visitors for international short courses and workshops. This space will include a dedicated computer lab and lecture hall, plus substantially faster Internet connectivity than has been available in previous years.

Program venue for DAIDD clinics

The DAIDD clinics will be held on the University of Florida's main campus in Gainesville, at the University of Florida's Health Science Center (HSC) Library, which provides convenient access to all of the services and technology needed for the Clinic. The HSC Library has a teaching classroom with 27 student computers and two 52 inch ceiling mounted monitors that project the screen from the computer at the instructional podium. Across the hall from the teaching classroom is the Library's Collaboration Center, which is equipped with a large conference table, a 65 inch interactive smart board/projector, and a 2-way teleconferencing facility. The library also has many spaces for group and individual work, including study rooms, a Collaboration Commons with group workstations, and quiet zones with tables and carrels. The Library is a 20-minute walk, or short bus ride, from the University's Reitz Union Hotel, where non-local faculty and participants will be provided with accommodations for the duration of the Clinic. DAIDD

will be held in December each year, allowing participants to take advantage of Florida's attractive winter sunshine, with daily temperatures ranging (on average) from a low of 46 to a high of 69 degrees. Location of the Clinics on UF's main campus will also allow participants to interact with researchers at UF's Emerging Pathogens Institute, a freestanding interdisciplinary research institute that draws faculty from across the University who focus on infectious diseases and has a strong modeling component.

Resources for I3D scholars

Resources for I3D scholars, including work space, computer access, and library access, will be arranged by the ICI3D faculty advisor at the faculty member's home institution. Faculty members will be required to confirm the availability of these resources prior to notification of I3D applicants that they have been selected for participation.

Justification of Foreign Involvement and Use of Multiple Sites

The international focus of the proposed ICI3D program has a two-fold purpose: on the one hand, the program aims to build capacity for population-level infectious disease research in the an area of the world with a very high infectious disease burden; on the other hand, the program aims to develop international ties for young American researchers, in recognition of the importance of building an American scientific workforce able to engage in an increasingly global environment. Use of multiple sites for the program will allow us to reach a broad audience of both American and African researchers and to effectively integrate these two groups of researchers into a single international research community. To reach the same number of African and American researchers using a single program site would be prohibitively expensive, regardless of the site used, due to the amount of intercontinental travel that would be required.

Multiple PD/PI leadership plan

The multiple PI structure for the proposed ICI3D program is intended to ensure committed leadership for the project from both the American and African sides of the collaboration. Dr. Pulliam will serve as the Contact PI and, as such, will be responsible for communication between the Program Directors and the NIH and for coordinating progress reports. She will also take primary responsibility for the execution and development of the DAIDD clinics and for the management of all North American aspects of the MMED clinics, including participant recruitment and selection but also travel for North American faculty and participants and annual updates to the program schedule in response to evaluation. Dr. Welte will take primary responsibility for coordinating local aspects of the MMED clinics, including participant recruitment and selection but also the evaluation process to be conducted by Dr. Hitchcock of SACEMA. Drs. Pulliam and Welte will share responsibility for the I3D scholarship exchange program. Dr. Puliiam will coordinate the nomination and selection processes, in close collaboration with all ICI3D faculty, and will be responsible for overseeing logistical arrangements on the North American side. Dr. Welte will be responsible for overseeing logistical arrangements on the African side. The two PI's will communicate frequently by email and phone.

Should a dispute arise within the ICI3D faculty or staff, Drs. Pulliam and Welte will work together to mediate the dispute and reach a satisfactory solution. If the dispute cannot be resolved internally, the Program Directors will seek mediation through the appropriate institutional pathways at the University of Florida and Stellenbosch University. Should a dispute arise between Drs. Pulliam and Welte, the Program Directors will attempt to resolve the dispute through discussion with Dr. Dushoff, who will act as an impartial intermediary. If the dispute cannot be resolved internally, the Program Directors will seek mediation through the appropriate institutional pathways.

Consortium/Contractual Agreements

The ICI3D program will be run through two Consortium institutions and two institutional partners. The Consortium consists of the **Emerging Pathogens Institute** (EPI), which is an interdisciplinary research institute based at the University of Florida, and the **South African Centre for Epidemiological Modelling and Analysis** (SACEMA), which is a National Centre of Excellence funded by the South African government and affiliated with Stellenbosch University. The primary institution receiving and responsible for the grant funds will be the University of Florida, and SACEMA will receive funds through a subcontract, as outlined in the sub-award budget attachment. The total amount of this sub-award over the full grant period will be $184,081 (combined direct and indirect costs). The subcontract includes salary and fringe benefits for 1 ICI3D faculty member (Hargrove, 0.05 FTE), the evaluation expert (Hitchcock, 0.05 FTE), and clerical support (0.10 FTE); travel and room and board costs for 3 Africans mentors to attend MMED each year (see the Research Education Program Plan for a description of the mentors program), room and board costs for the 8 American MMED participants per year, and local transportation costs.

In addition to the funds provided to SACEMA through the sub-award, over the course of the full grant period SACEMA will contribute approximately $175,000 from its core funding to cover additional expenses associated with the MMED clinics, as described in the letter of support from Dr. Alex Welte (Director of SACEMA and a Program Director for the proposed ICI3D program). The expenses covered from SACEMA core funding are primarily in the form of support for African participants (approximately 20 per year) but also include other local costs in South Africa, such as excursions arranged for participants, plus salary for some ICI3D faculty and staff (Welte, Delva, Williams).

The ICI3D program's institutional partners are the **African Institute for Mathematical Sciences** (AIMS) in Muizenberg, Cape Town (South Africa) and **Colby College** in Waterville, Maine (USA). Each of these partners will contribute to the success of the program by providing services and/or covering costs associated with the program.

AIMS will host the annual MMED clinics, as it has been doing for the Clinics and precursor programs since 2007. In return for services provided, AIMS will receive $2,000 each year of funding from the grant, to be invoiced to the University of Florida (see budget justification for further details). In addition, AIMS will support approximately 10-20 local MMED participants each year; however, the support for these participants – who are students and researchers already based at AIMS – does not go beyond the support these individuals would receive from AIMS in the absence of the Clinic, so this support is not counted in the total in-kind contribution amount provided by non-federal (US) funds for this program.

Colby College Dr. Scott to allocate substantial time and effort to participation in the ICI3D program without charging his salary for this time to the grant. Over the full grant period, these contributions total approximately $18,500. This agreement is confirmed by a letter of support from Colby's Dean of Faculty.

Resource Sharing Plan

One of the specific aims of the ICI3D program will be *to create open access resources for training in data-driven modeling of infectious disease dynamics*. To this end, we will create, distribute, and maintain a package for the statistical programming language R that contains all of the R-based computer tutorials used in the MMED and DAIDD clinics. The R package and other instructional materials will be made available via open access licensing. Instructional materials from the 2010 and 2011 MMED clinics are already available for free download under Creative Commons licenses and can be accessed through the current MMED website (http://lalashan.mcmaster.ca/theobio/mmed).

This proposal also includes funding for further development and maintenance of the WorkingWiki extension to the MediaWiki project, including modification of the WorkingWiki extension to tailor it to the needs of the ICI3D research community. The current version of the WorkingWiki extension and its source code are available for free download from http://lalashan.mcmaster.ca/theobio/projects/index.php/WorkingWiki. Future modifications of the WorkingWiki exntension created under this grant will also be made available via open access licensing.

Importantly, the current MMED clinics rely entirely on open access software – including the Open Office spreadsheet program Calc, the statistical programming language R, and the WorkingWiki extension to the MediaWiki collaboration environment – allowing all participants to continue projects started at the workshops upon return to their home institutions. We are fully committed to the open access model.