# **DIMACS Center Rutgers University**

# Workshop: Facing the Challenge of Infectious Diseases in Africa: The Role of Mathematical Modeling Johannesburg, South Africa

**Final Report** 

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#### Participants who spent 160 hours or more

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#### **Other Collaborators:**

The project involved scientists from numerous institutions in numerous counties. The resulting collaborations also involved individuals from many institutions in many countries.

#### **Partner Organizations:**

African Institute for Mathematical Sciences (AIMS): Collaborative Research Individuals from the organization participated in the program planning.

South African Centre for Epidemiological Modelling and Analysis (SACEMA): Collaborative Research Individuals from the organization participated in the program planning.

School of Computational and Applied Mathematics, University of the Witwatersrand: Collaborative Research

Individuals from the organization participated in the program planning.

AT&T Labs - Research: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

Alcatel – Lucent Bell Labs: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

Avaya Labs: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning. Georgia Institute of Technology: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

HP Labs: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

IBM Research: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

NEC Laboratories America: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

Microsoft Research: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

Princeton University: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

Rensselaer Polytechnic Institute: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

Stevens Institute of Technology: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

Telcordia Technologies: Collaborative Research Partner organization of DIMACS. Individuals from the organization participated in the program planning.

# Activities

The main activity of this project was a workshop. However, with funds remaining from the workshop, we also were able to enhance two following activities, an advanced study institute and a capstone workshop following the Institute.

#### THE MAIN WORKSHOP

# Workshop: Facing the Challenge of Infectious Diseases in Africa: The Role of Mathematical Modeling

Dates: September 25 - 27, 2006
Location: University of the Witwatersrand (Wits), Johannesburg, South Africa
Organizers: Dominic Clemence, North Carolina AT&T State University; Wayne Getz, UC Berkeley; Abba Gumel, University of Manitoba; John Hargrove, SACEMA; Edward Lungu, University of Botswana; Fred Roberts, DIMACS
Attendance: 58

DIMACS, in collaboration with SACEMA (the South African Centre of Excellence for Epidemiological Modeling and Analysis), held a 3-day workshop on mathematical modeling and infectious diseases in Africa. The workshop was at the School of Computational and Applied Mathematics at the University of the Witwatersrand (Wits), Johannesburg, South Africa, on September 26-28, 2006. The workshop provided an agenda for future collaborations between U.S. and African scientists. It exposed junior U.S.

scientists and students to the special challenges of modeling the spread of disease in Africa. It also provided them with opportunities to collaborate with Africans in developing and applying the tools of mathematical modeling to the tremendous health problems caused by such diseases as HIV/AIDS, tuberculosis and malaria, as well as to the possible interventions when major new health threats such as pandemic influenza threaten a developing region of the world.

Endemic and emerging diseases in Africa provide new and complex challenges for mathematical modeling. The participants included scientists and public health practitioners, as well as junior researchers and students, from the U.S. and various African countries. The 3-day workshop provided an opportunity for the 58 participants to share current understandings of disease modeling, and discover new perspectives that may help to combat the spread of emerging and re-emerging diseases. Participants were provided with the opportunity to forward an agenda for future workshops and encouraged to develop collaborations aimed at using mathematical methods to address the severe public health and socio-economic burdens inflicted by disease in Africa. By facilitating dialogue between scientists from developed and developing countries, each group was directly exposed to the real-world differences between facing diseases in resource-rich and resource-poor societies. Africa's unique environments, cultures, politics, religions, stigmas, and ethics must be factored in to public health initiatives if they are to be successful. Similarly, modelers must include knowledge of these differences in order to understand and overcome the difficulties associated with data acquisition, data sharing, model development, policy recommendation, and practical implementation in a wide range of health scenarios. Most importantly, the workshop provided an opportunity for U.S. and African scientists to interact and share information. This is an achievement that should not be overlooked or underestimated, as scientists across Africa often work in isolation, with few institutions providing the facilities required to develop inter and intra-continental collaborations (which makes this important in its own right) and few U.S. and African scientists have had the opportunity to interact in this way in this field. The public health community is increasingly reaching out to mathematical modelers to provide much needed assistance in disease program design. Modelers are now considered important allies in formulating strategies to manage a range of infectious diseases, including: HIV and HIV co-infections, tuberculosis, malaria, sexually transmitted infections, human papilloma virus, cervical cancer, pneumococcus, hepatitis B, dengue hemorrhagic fever, and a variety of animal diseases. Mathematical modeling can make a substantial contribution towards understanding the disease transmission dynamics, recommending suitable forms of data acquisition and interpretation, and formulating public health policies and practice. These activities require careful operations research and optimization for successful delivery, especially in resource challenged settings, and so remain top priorities for providing better health care.

There were four topic sessions held over three days: discussions on the current state of infectious disease in Africa and the subsequent special challenges for mathematical modeling; the role of mathematical modeling of diseases that inflict a significant burden on Africa, specifically HIV / AIDS and other diseases; the optimization of scarce public health resources; and modeling issues arising from the threat of emerging diseases in resource-poor countries, including pandemic flu and vaccination strategies. A few of the highlights of the workshop are described below.

At the start of the workshop, John Hargrove, DST/NRF South African Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA), introduced the newly formed SACEMA, an institution with a mandate to promote epidemiological modeling and analysis in South Africa, housed at the University of Stellenbosch in the Western Cape. Understanding and controlling epidemiological processes requires development of innovative mathematical models and modeling techniques, and thus a reasonably high level of mathematical expertise. South Africa, like many other developing countries, is relatively weak in this technical area. SACEMA aims to: 1) complete work in the field of mathematical epidemiology that contributes substantially to the alleviation of the effects of major diseases and 2) strengthen sustainable capacity in South Africa by facilitating and funding: a) research by international

and local scientists, b) training opportunities for young mathematicians interested in this field, c) visiting fellows to contribute to research and capacity building initiatives, and d) workshops and summer schools to collect small numbers of interested, talented individuals to focus intensively on a given modeling problem. Of particular emphasis is the development of African scientists and students.

Hargrove discussed some of the fundamental problems in the modeling of HIV epidemics that, on occasion, lead major agencies that advise African governments to arrive at inappropriate conclusions about trends in the epidemic. He discussed the uncertainties associated with reports of HIV prevalence in the greater Harare region. Research conducted by the CDC suggested no change in HIV prevalence after about 1994/1996. This is in contrast with recent findings that suggest that HIV prevalence has been declining since at least 1998, and incidence perhaps as early as 1994. This discrepancy can be blamed on inadequate data, as well on incomplete models. SACEMA will (as much as possible) play an active role in data acquisition, processing and secure storage, in an attempt to ensure access to good data for SACEMA projects, and for a wider modeling community.

John C. A. Davies, School of Public Health, University of the Witwatersrand, South Africa, shared his vast experience in the public health sector of southern Africa, focusing on his experience with tuberculosis control in Zimbabwe. His talk encouraged much discussion and highlighted many issues that mathematical modelers will face when working on problems in this region. This is due to Africa's unique environments, cultures, politics, religions, stigmas, ethics, and so on. Mr. Davies reported that there have been several oppressive developments in public health. The obsessive pursuit of treating established disease consumes almost all the available resources. A highly centralized bureaucracy effectively restricts freedom of action, rural health professionals work without support, and politicians and human rights lawyers have usurped a public health function. The countries of southern Africa face an unprecedented public health crisis. Davies asserted that control of the conjoined epidemics of tuberculosis and HIV/AIDS requires a complete break with the past and, in particular with the emotional and political baggage accumulated around HIV and tuberculosis in South Africa in the past decade. The following questions were discussed: 1) what is driving the epidemic of tuberculosis and 2) what do we need to do in order not to fall into the trap of doing more of the same and failing again? Discussion focused on the risk groups of the dual epidemic. Although the risk group in a general epidemic is much smaller than the nonrisk group for most diseases (plague, smallpox, measles), this is not the case for TB in South Africa, where the large number of salica exposed mine workers may be part of the reason for failing to control the disease. Public health interventions need to be evaluated against a properly constructed mathematical model, which will tell us exactly where we are going in controlling disease, and how fast.

Diana Dickinson, Physician and Director of Medical Services, Family Medical Practice, Botswana, presented a clinical overview of the state of infectious disease in southern Africa from a Bostwanan medical doctor's perspective. She emphasized the problems, challenges, and social costs of disease in a developing world scenario, along with some new initiatives. Recommendations for mathematical modelers were given about planning, changing policy, and evaluating disease, with specifics for a number of diseases, including HIV, tuberculosis, pneumococcus, malaria, hepatitis B, herpes, cervical cancer and Karposi sarcoma.

HIV / AIDS: According to Dr. Dickinson, approximately 40 million people were living with HIV in 2005 (2.3 million children), with 4.1 million new infections and 2.8 million deaths recorded in the same year. Over one-third of these deaths were in southern Africa, highlighting the potential impact of this disease in the region. Life expectancy has sharply declined as a result. Access to antiretroviral treatment varies widely from 75% coverage in Botswana, to less than 10% of those in need in Zimbabwe. Dr. Dickinson stated that the big change in Botswana's policy was aided by two reports that used mathematical models to predict the effects of the disease.

Tuberculosis: According to Dr. Dickinson, the global TB incidence continues to grow at 1% per year. In 2003, 9 million new cases of TB and 2 million deaths were reported, with the risk of TB infection at 5-15% per year in HIV positive patients, 50 times the risk of those who are HIV negative. 30-40% of all HIV deaths in Africa are due to TB, as the risk of TB doubles in the first year of HIV infection. This affects a wide section of society, including the medical profession.

Dickinson summarized by saying that medical practitioners need to influence policy and predict the changing faces of disease. They need to evaluate different prevention strategies and interventions, and to prioritize many aspects of public health care and service. Program planning requires information on many things, including the costs of prevention, testing, treatment, diagnostics, and disease monitoring. Human resource managers need to calculate the number of health workers needed and the associated costs of employing and training more health workers.

Social care programs are also necessary, but are expensive. Evidence is therefore needed on how best to manage these different aspects of medical care. It is within these frameworks that mathematical modelers could be ultimately helpful in painting fitness landscapes and helping assess the priorities for an ever expanding health service demand, something that over-worked and under-resourced doctors simply cannot do in the current situation.

Abba Gumel, University of Manitoba, Canada, presented some results, issues and challenges in modeling transmission dynamics of HIV/AIDS. Since its emergence in the 1980s, the HIV/AIDS pandemic continues to pose an unprecedented threat to global health and human development. An estimated 34-46 million people are currently living with the virus, and over 20 million people have died due to AIDSrelated causes over the last two decades. In addition to the enormous socio-economic burden it imposes, AIDS is now the leading cause of death in sub-Saharan Africa, and has cut the life expectancy in a number of countries in this region. Gumel addressed mathematical modeling issues and challenges associated with evaluating established and new strategies for curtailing the spread of HIV in resourcepoor nations. Another issue crucially important to modeling HIV spread in Africa is its interaction with other curable pathogens (opportunistic infections) such as mycobacterium tuberculosis and malaria. The key question here is how limited public health resources should be distributed between managing curable opportunistic infections and controlling HIV, and how an optimal result may be achieved when optimizing with respect to "burden of disease" measures. A discussion about male circumcision (MC) campaigns highlighted the responsibility that programs have in assuring that reduced risk in acquisition of HIV after successful MC should not lead to a false sense of protection resulting in an overall increase in risky behavior. The high number of fatalities and other adverse side effects of traditional MC procedures highlight the responsibilities of programs to provide MC procedures by trained medical personnel along with appropriate post-surgical follow-up.

Fred Roberts, DIMACS, discussed the new challenges for modelers of infectious diseases of Africa, the role of discrete mathematics, and the DIMACS initiatives. Roberts outlined the background for this workshop and provided an introduction to the past goals and potential future roles of DIMACS. He described the main themes of the meeting, including the special modeling challenges arising from African diseases and the issues raised by emerging diseases in resource-poor countries. DIMACS aims to bring together U.S. and African researchers and students to collaborate in addressing the problems of public health and disease with regard to epidemiological modeling. Workshops, tutorials, working groups and exchange programs will help to achieve these aims. Today's endemic and emerging diseases provide a new and complex challenge for mathematical modeling, especially in developing countries. Modeling can also play an important role in shaping public health policy decisions as can be seen in developed nations like the UK, U.S., Netherlands and Canada. It can provide insights leading to "optimal" treatment strategies and vaccine design and use. During the SARS outbreaks in 2003, modelers and public health officials worked together to devise effective control strategies in a number of countries. This illustrates

the new methods and approaches that are needed to deal with the large size and complexity of modern epidemiological problems. These include addressing the dynamics of multiple interacting strains of viruses through the construction and simulation of dynamic models; studying the spatial spread of disease through pattern analysis and simulation; and the early detection of emerging diseases or bio terrorist acts through rapidly responding surveillance systems. In order to gain the maximum benefit from mathematical models they must be specialized: tested to ensure that the assumptions are correct in specific contexts and populations, with local data used to help define the key parameters. In addition, by encouraging scientists from developing countries to participate, access to data and relevant interpretation would be improved, yielding better and more realistic models. It is important for non-Africa researchers to understand the effects of government policies in Africa on the current state of infectious diseases in Africa.

Aspects of disease specifically relevant to resource-poor countries include problems relating to slow communication, the short supply of vaccines and prophylactics, and the difficulty of imposing guarantines. Models have therefore been used to optimize scarce public health resources, allocate medicines, assign trained personnel to the most critical jobs, and design effective transportation and dispensing plans. Additionally, computer simulations have been developed to compare vaccination strategies where field trials have been prohibitively expensive. Training programs for African and non-African students need to be developed to ensure the future of such work and initiatives. Many mathematical tools have been used in epidemiological modeling, but the usefulness of newer tools of discrete mathematics and algorithmic methods of theoretical computer science have not yet been widely used in mathematical epidemiology. Statistical methods have been used to evaluate the role of chance and confounding associations, and to find sources of systematic error in observations. However, due to the increasingly large data sets involved, new approaches will be needed, which was a further point of discussion in this presentation. Dynamical systems have been used for modeling host-pathogen systems and phase transitions when a disease becomes an epidemic. They use difference and differential equations but require powerful computational tools. Probabilistic methods use stochastic processes, random walk models, percolation theory and Markov chain Monte Carlo methods, Computational methods for simulating stochastic processes in complex spatial environments or on large networks have been used to simulate more complex biological interactions. Discrete mathematics and theoretical computer science (TCS) methods have been used in many fields of science, and particularly in molecular biology. However, few have been used in epidemiology and mathematical epidemiology. When combined with geographic information systems (GIS), large and disparate computerized databases relevant to a disease can be combined via data mining techniques. TCS methods have also been used to construct phylogenetic trees based on evolutionary principles as they deal with arrangements, designs, codes, patterns, schedules and assignments. Unfortunately, these tools, which seem especially relevant to problems of epidemiology, are not well known to those working on public health problems. One type of analysis based on these principles is cluster analysis, which extracts patterns from complex data. Traditional clustering algorithms are hindered by extreme heterogeneity of the data but newer methods need to be modified for infectious disease applications. Visualization of the data can help, but algorithms become harder to develop when data is extracted from various sources. The data also often requires cleaning due to poor manual entry, lack of uniform standards, data duplication and measurement errors. TCS-based methods of data cleaning can help remove duplicated records automatically.

Roberts described some aspects of modeling disease transmission via the social network method. Contact information is often key in controlling an epidemic, and the use of discrete mathematical tools can help interpret these networks as graphs. Research issues include making use of other information about networks (e.g. semantic graphs), approximating parameters such as infectivity, susceptibility, and latent periods that are not well specified, and making use of analogous lines of research such as the spread of opinions or education through social networks. The discussion of models of evolution suggested that these may help shed light on new strains of infectious agents and new methods of phylogenetic tree

reconstruction may help identify the source of an infectious agent. Some relevant tools of discrete math and TCS might be disk-covering methods, nearest neighbor joining methods, and hybrid methods. One of the most important aspects of modeling infectious disease will be in aiding decision-making and policy analysis in under-resourced areas. Mathematical models can help with understanding fundamental processes, comparing alternative policies and interventions, providing a guide for scenario development, guiding risk assessment, and predicting future trends. Operations research, used in military decisionmaking, may be of use in allocating scarce resources to different components of a health program. Combinatorial group testing may be used when natural or human-induced epidemics require testing large populations. Roberts concluded by saying that the purpose of this DIMACS workshop was to survey new methods and discuss new approaches for mathematical epidemiology, open up new lines of communication, and lay the groundwork for future collaborations.

Senelani Dorothy Hove-Musekwa, National University of Science & Technology, Zimbabwe, talked about the role of mathematical modeling in epidemiology, with particular reference to HIV/AIDS. She focused on some real-world implications of HIV/AIDS and highlighted the role of mathematical modeling in helping to provide decision makers with measures of intervention program success and predictions of future problems. AIDS is a fatal disease for which the cause is known and the principal routes of transmission understood. As the prospects for curative therapy or effective vaccines are poor, governments, public-health agencies, and health-care providers must determine how best to allocate scarce resources for HIV treatment and prevention. Control of the epidemic depends on promoting behavioral change among the subgroups of populations where infection is taking place and on optimum use of available therapy for those infected. By identifying HIV causal and preventive factors through systematic investigation of different populations and subgroups over time and space, these can be placed into a mathematical model to assist with disease program development. It is important to understand the health problems, the characteristics of the disease, the demographics of vulnerable populations, and the location and time factors associated with outbreaks. This is with a view that information and modeling outputs will be effective and lead to improvements in health status and care. It is therefore key that a model have explicit assumptions and testable predictions, a framework for data analysis, projections, and various intervention possibilities.

Hove-Musekwa described previous models to show that treatment of HIV-1 infection during the symptomatic phase has significantly improved patient survival. She presented a two-strain HIV mathematical model that captures the dynamics of the immune system and two HIV-1 variants under antiretroviral therapy. Discussion concentrated on how data was used to validate the model, and the difficulties involved with understanding the interplay between variables that cause and affect infection. In this case, it is important to know how to evaluate the models, and it was particularly suggested that students be taught the wider aspects of mathematics and not just statistics. Teaching courses on the transmission dynamics of disease and employing some mathematical content in the training of medical doctors and public health officials would be helpful. Collaboration between health workers, statisticians and mathematicians should also be intensified. Further questions included how treatment with interruptions or stopped treatment responded in the model. This had not been tested at this stage, although wild type elements had been shown to die.

Ramanan Laxminarayan, Resources for the Future, gave insights from economic epidemiology. Laxminarayan tackled an essential aspect of disease and epidemiology: how to conceptualize the interplay among economics, human behavior, and disease ecology to improve our understanding of the emergence, persistence, and spread of infectious agents. He considered ways to delineate the most optimal strategies and policies to control the spread of disease, i.e. how best to deploy scarce resources for disease control when epidemics occur in different but inter-connected regions, or when individuals adapt to the threat of infection by adopting protective measures. Major points discussed included an individual's response to disease (the decision to be vaccinated, treated, or tested, physiological responses to drugs and resistance), as opposed to major government response (wait until it is a public health problem or prevent infections initially). These actions factor in to the public price subsidy argument. For example, if those who choose to invest in a medical program get vaccinated this may in turn reduce the incentive for those outside the program to comply with regulations as they are at a decreased risk of exposure to disease since the majority of people are protected. Subsidies may also increase the number of people who will pay to be tested for a disease but this has no bearing on the behavior of individuals after the knowledge of the test result and the potential for infectivity of other susceptible individuals. Additionally, monopolistic vaccine manufacturers may have little incentive to eradicate disease, as the market for their product would disappear with disease eradication.

Disease complementarities provide an incentive to invest in preventing one cause of death (for example HIV) only if you are sure you are not going to die from something else (TB). This can be translated into the need for regionally coordinated disease control for hospitals to offset the possibilities of outbreaks in areas close to those where a heavy investment in prevention has been made. On a regional scale, at low levels of infection in different populations, it is preferential to treat the populations with a higher transmission coefficient because of the greater economic value associated with greater potential to prevent secondary infections. However, at high levels of regional infection, it is preferential to treat the populations with lower levels of infections since the higher probability of re-infection in high infection populations reduces the economic value of the treatment. It was also noted that a combination of quarantine with preferential treatment of a less infected region could bring explosive disease under control. In summary, mathematical models that capture the complex interplay between economics, human behavior, and disease ecology may be more helpful in understanding how diseases evolve and spread than models that rely on epidemiology alone. Group discussion raised a number of points. Measuring secondary impacts of disease on societies is difficult and hard to quantify. It is equally difficult to factor in individual behaviors and cultural aspects to health service use. For example, the compulsory immunization of children in Zimbabwe would not work in Rwanda, where laws and traditions are very different and no medicine that is left over may remain in the house. It is therefore important to consider local traditions when constructing models of behavior and economics.

Other talks were presented by:

Alex Welte, University of the Witwatersrand Edward Lungu, University of Botswana David Hill, Stanford University Frances M Cowan, Royal Free and University College Medical School, Univ. College London Asamoah Nkwanta, Morgan State University Claire Geoghegan, University of Pretoria and Wayne Getz, UC Berkeley Derek Cummings, Johns Hopkins Bloomberg School of Public Health Aziz Yakabu, Howard University Philip Johnson, UC Berkeley Gerardo Chowell-Puente, Los Alamos National Laboratory Miriam Nuno, Harvard School of Public Health Swati B Gupta, Merck Research Laboratories Elamin Elbasha, Merck Research Derek Cummings, Johns Hopkins Bloomberg School of Public Health and Univ. of Pittsburgh John Glasser, CDC Michael Washington, CDC Nina Fefferman, DIMACS and Tufts University

There was a panel on "Next Steps" chaired by Abba Gumel, University of Manitoba, with panelists: Diana Dickinson, Family Medical Practice, Botswana, Fritz Hahne, AIMS, John

Hargrove, SACEMA, Fred Roberts, DIMACS, Alex Welte, University of the Witwatersrand, and Frances Cowan, Royal Free and University College Medical School, Univ. College London. There were 26 posters in the poster sessions and this was very well attended by the all the participants. In addition, there were breakout sessions with discussion groups that later developed reports with recommendations for next steps. The discussion group topics were:

Epidemiology in Africa and its Unique Challenges for the Modeler Mathematical Modeling of Diseases with a Particular Burden on Africa Modeling Issues Arising from the Threat of Emerging Diseases in Resource-Poor Nations Optimizing the Use of Scarce Public Health Resources Professional and Mid-Career Development, Workforce and Collaboration

In summary, this three-day workshop of individual presentations and group discussions successfully brought together mathematical researchers, medical professionals, clinicians, ecologists, microbiologists, economists, laboratory scientists, pharmaceutical industry representatives, operations researchers, public health officers, students, and members of both government and non-government organizations. A deeper understanding regarding the needs for endemic and emerging disease control was achieved, especially with regard to the unique challenges faced by developing countries. It was also recognized that Africa is a continent that encompasses a range of cultures and environments. Consequently, mathematical models should be adapted for each individual environment based on the input of local scientists and stakeholders. This enhances the credibility and usability of any developed models, especially from the point of view of public health users. One step towards achieving this was taken by having this workshop, which integrated the perspectives of African regional scientists with those with developed western backgrounds. Recommendations for the direction of future work and research were discussed, and included the following:

Epidemiological modeling should maintain a wider focus to enable local factors to be included in model development. Examples include regional drivers of disease like migration, co-morbidity, malnutrition, and conflict. Additionally, capacity analysis should be encouraged, which, for example, may be essential for successful vaccine rollout.

Measures of disease costs should incorporate the level of direct burden placed on a country, and not simply the monetary costs. This includes developing uncertainty analysis and optimization strategies for parameters including salaries, drugs, infrastructure, facilities, etc.

Simple guidelines for data collection and storage and the standardization of measures (including medical, social, economic etc.) should be produced. This will help prevent the duplication of efforts required for data collection, ensure data is in a consistently useable form, and prevent the loss of information, all problems experienced in disease management.

It was felt that the specific goals for the participants as they go forward should be to enhance the advancement of mathematical and epidemiological training for a range of interested stakeholders and to promote interdisciplinary science. This could take the practical form of offering courses and workshops for professional and student development and also of facilitating greater interdisciplinary collaboration. This would help to establish greater communication between scientific groups and with local communities. This in turn would help to maintain a degree of momentum and continuity of thought over time. It is also hoped that greater collaboration between African scientists with those elsewhere will aid in the dissemination of results based on the work presented during the workshop.

Finally, it was felt that the participants should aim to develop support collaborative research and workshop attendance through the allocation of funding for scientists and students from resource-poor areas.

Overall, this workshop was a very successful event that facilitated the ongoing collaboration between U.S. and African scientists. It is hoped that further meetings will continue this work and ultimately contribute towards the effective and applicable modeling of infectious disease in Africa.

# SUGGESTIONS FOR NEXT STEPS

Based on discussion groups and the exit questionnaire, we gathered suggestions for "next steps." The suggestions clustered around five areas: 1) providing student training at all levels but especially on the graduate level, 2) providing support for ongoing collaborations and broadened participation, 3) involving even more people outside of mathematics and science, especially public health officials, 4) supporting even more cross-disciplinary interactions, and 5) discipline specific suggestions. Below are some representative comments.

### Provide student training

"I would suggest some formal effort to encourage the training of Epidemiology students in the US, who want to understand this stuff but often have few opportunities to do so."

"Adding (infectious disease) Epi training short course for students such as those at AIMS. I would volunteer to do some teaching (D. Hill) in order to get technically trained students to get informed about public health challenges and excited about being involved in solutions."

"It would be helpful also to have short courses to improve and stimulate knowledge in the area and develop skills to enable high interaction and identify problems."

"Workshops with a teaching component for graduate students including projects done by students. Get African institutions to support African students. NEPAD should be approached for funding. Emphasize co-supervision of graduates."

"Short courses for African students on specific topics."

"Train young mathematicians, especially Africans, to improve their productivity."

"Outlining the actual steps for modeling. How to develop a problem or dissertation topic in MathBiology. Emphasis on tools (software) and other techniques used in research."

"Explore the possibility of starting to influence school education in South Africa with a view, particularly, of improving math education."

"Creating an REU math-bio program in South Africa or the continent in general. Sending students to an REU in the U.S. really isn't cost effective."

# Support collaborations

"Increase the participation of black researchers/students, maybe in the form of capacity building. Increase links and collaborations among researchers. Include east and central Africa as it is linked to southern Africa."

"It would be great to build on possible collaborations and support their development by providing short visit programs for student-faculty pairs to follow up on work together. Maybe 1 trip for each to the other?'

"Perhaps have a student-focused workshop to encourage more participation from local students (multi-African). Also, South African technical college students are often ignored but tend to have courses that encourage application of knowledge in the real world."

"It would be good to hear from the students in regards to what they would like to suggest for next steps. A student group session might be useful where they could report their concerns or interests to the workshop organizers."

# Involve people outside of academics

"Participation of more public health officials, particularly coming from government agencies." "Encourage attendance of public health & clinical professions. Also, are there government statisticians who could be invited to comment on how they currently use national data to model & predict health/population trends?"

"Physicians, especially public health physicians, need to be fully involved. The first step is inviting them for a course on the basic concepts of modeling, presenting examples of applications of modeling in public health practice. Improve on surveillance systems by training data managers. Run short courses for public health physicians and policy makers. Have workshops for traditional healers. Run a course on operational research in health care for managers, policy makers, physicians, and interested graduate students."

"Involving more people in policy/public health. People 'on the ground' can tell modelers what to focus on, while modelers can share their results with the real world."

"Having Diana Dickenson here, as a clinician, was great but having a couple of field people (doctors, public health workers) would be very valuable as a complement to all of us theory folks."

Explore "the area of collaboration between mathematicians and clinicians."

"I think having political leaders with scientists would be helpful in making decisions."

"Might look at including civil servants with a view to influencing policy."

"Encourage greater participation of (more) public health officials."

"Each discussion group needs at least one clinical facilitator to ground the discussion in experience and practice from the field and to give opinions as to what is vitally important for modelers to focus on."

# Support cross-disciplinary interactions

"Work with other societies to bring in researchers with the background we need. Include more isciplines" "I think it's a good idea to make a link between fundamental science and mathematical models like pathogen's genotype and predictive drug resistance such as in HIV disease or TB."

"One need is that it seems some mathematicians have little to no disease-specific knowledge and their models are frequently academic exercises, not intended to solve pressing problems of disease in Africa. We must educate the mathematicians in substantive health knowledge. For example, I talked to one mathematician who had never heard of PubMed. That must change."

"Suggest include demographers with interest in impact of disease."

"Emphasize modeling efforts in animal diseases and impact of climate change."

# Discipline specific suggestions

"Look at optimizing direct resources instead of global resources."

"More explicit discussion of mathematical issues in laboratory data analysis."

"The next step in the SACEMA-DIMACS collaboration is to increase the proportion of models based on real data and thru these into intervention strategies."

"Take positive steps to improve access data to be used in Epidemiological modeling in Africa."

"More focus on particular diseases or problems might work better, for instance, modeling interventions for reducing HIV transmission or focus on drug resistance in TB & malaria."

# FOLLOW-UP ADVANCED STUDY INSTITUTE AND WORKSHOP

The feedback from this workshop informed and guided our development of an Advanced Study Institute for graduate students and a following capstone workshop for the Institute students together with senior researchers. This was supported under a separate grant for which a report has already been submitted. The project being reported on here allowed us to increase the number of U.S. students we were able to accept for the Advanced Study Institute and the capstone workshop from among an outstanding group of applicants. The Institute and workshop are described below.

### US-Africa Advanced Study Institute on Mathematical Modeling of Infectious Diseases in Africa Dates: June 11 - 22, 2007

Location: AIMS, Muizenberg, South Africa Organizers: Brenda Latka, (Program Chair), DIMACS; Wayne Getz, UC Berkeley; Abba Gumel, University of Manitoba; Fritz Hahne, AIMS; John Hargrove, SACEMA; Simon Levin, Princeton University; Edward Lungu, University of Botswana; Fred Roberts, DIMACS; Alex Welte, Wits University

Attendance: 46

DIMACS, in collaboration with SACEMA and AIMS, held a two week Advanced Study Institute on mathematical modeling and infectious diseases in Africa, culminating in a 3-day capstone workshop.

The DIMACS/SACEMA/AIMS Advanced Study Institute provided a select group of graduate students the opportunity for exposure to a field where there is a critical shortage of people with the necessary high-level skills and which has many exciting opportunities for research and practical application. The institute trained United States and African graduate students in mathematical epidemiology and the control of emerging and re-emerging diseases. The capstone workshop enabled Institute students to interact and establish collaborations with United States and African researchers who are currently actively involved in the modeling of diseases in Africa.

The students were selected by a highly competitive process. Each student submitted an application describing their background and interests, a letter of recommendation, and a letter of commitment from a mentor to support the continuation of the research project begun during the Institute or a new project begun afterward. Twenty-two of the students selected for the Institute were from the United States and twenty-four from Africa, creating an opportunity for establishing early collaborations between these junior researchers.

The Institute consisted of a series of lectures and tutorials on the design and analysis of models for the spread of emerging and re-emerging diseases. The first week provided a basic introduction to mathematical modeling in epidemiology at a fast pace. This introductory week was designed to allow students who have never taken an epidemiological modeling course to acquire the necessary preparatory background they needed for the second week. The second week covered more advanced material. Various modeling paradigms were discussed, as well as introductory lectures on related topics. There were a number of hands-on and computer exercises together with group projects to reinforce and extend the various concepts covered. Participants submitted proposals for research projects they would complete after the Institute, under the supervision of a mentor.

The institute was held at the African Institute for Mathematical Sciences (AIMS), located in Muizenberg, a small seaside suburb of Cape Town and an area of outstanding natural beauty. Lecturers and students all lived and dined at AIMS, allowing for maximal contact time in an informal and collegiate setting.

Workshop: Mathematical Modeling of Infectious Diseases in Africa Dates: June 25 - 27, 2007 Location: Stellenbosch, South Africa Organizers: Brenda Latka, (Program Chair), DIMACS; Wayne Getz, UC Berkeley; Abba Gumel, University of Manitoba; Fritz Hahne, AIMS; John Hargrove, SACEMA; Simon Levin, Princeton University; Edward Lungu, University of Botswana; Fred Roberts, DIMACS; Alex Welte, Wits University Attendance: 74

DIMACS, SACEMA, and AIMS held a 3-day workshop on mathematical modeling and infectious diseases in Africa. The workshop brought together scientists and students from the U.S. and Africa. The aims of the workshop were to further research on the modeling of diseases in Africa and identify future research challenges. This workshop served as a capstone to an Advanced Study Institute, held at AIMS in Muizenberg, South Africa, on June 11-22, 2007, to train graduate students and postdoctoral fellows from the U.S. and Africa in mathematical epidemiology and the control of emerging and re-emerging diseases. The students who participated in the Advanced Study Institute were prepared by the Institute to participate fully in the workshop.

Mathematical modeling has provided new insights on important issues such as drug-resistance, rate of spread of infection, epidemic trends, and effects of treatment and vaccination. Yet, for many infectious diseases, and in particular many diseases affecting Africa, we are far from understanding the mechanisms of disease dynamics. The modeling process can lend insight and clarification to data and theories. To get the maximum benefit out of mathematical models, however, one needs to specialize them, test assumptions in specific contexts and populations, gather local data to help define key parameters, etc. This workshop developed collaborations and communications among U.S. and African senior and junior researchers on these issues, to benefit both sides in their research and the important public health applications of that research.

# STUDENT PARTICIPANTS IN THE ADVANCED STUDY INSTITUTE AND CAPSTONE WORKSHOP

This project contributed to the support of the following students to attend the Advanced Study Institute and the following capstone workshop:

Shweta Bansal, University of Texas, Austin Steven Bellan, UC Berkeley Ashley Crump, Howard University Lily Davidoff, NJIT Dylan George, Colorado State University Moses Haimbodi, Lincoln University Chris Langhammer, Rutgers University Devroy McFarlane, Howard University Akongnwi Mformbele, Lehigh University Sean Moore, Oregon State University Anthony Ogbuka, Morgan State University Anike Oliver, Howard University Camisha Parker, Virginia State Alex Perkins, University of California, Davis Sarah Radke, University of North Carolina Danielle Robbins, Arizona State University Sourya Shrestha, University of Michigan Althea Smith, North Carolina State

Evelyn Thomas, Howard University Alicia Urdapilleta, Arizona State University Holly Vuong, Rutgers University Nakeya Williams, Morgan State University

#### Findings

Evaluation of targeted influenza vaccination strategies via population modeling

John Glasser, CDC, Denis Taneri, National Health Command Center, Centers for Disease Control, Taiwan, William Thompson, CDC, Jen-Hsiang Chuang National Health Command Center, Centers for Disease Control, Taiwan, Jianhong Wu, Laboratory for Industrial and Applied Mathematics, York University, Peet Tüll, Scientific Advice Unit, European Centre for Disease Prevention and Contro, and James Alexander, CDC, developed a means of identifying sub-populations to target for vaccination, thereby using this scarce resource most efficiently. Annual influenza vaccine production schedules are tight and delays frequent, with supply shortages an increasing occurrence. Absent technological innovations, vaccine supplies are unlikely to suffice for entire populations during a pandemic, especially in Africa and Asia, where mutation or re-assortment facilitating person-to-person transmission of an avian or porcine strain is likely. Besides producers or distributors of influenza vaccines and anti-viral medications and providers of health care or other critical social services, who should have priority? In an age-structured model, in which inter-personal contacts are proportional to age specific activities alone or disproportionately within age groups, Glasser and his collaborators compared vaccinating infants and adults aged 65+ years, the current strategy, with vaccinating schoolchildren, an ofen suggested alternative. Where contacts are proportional to activity, a distributed quantity peaking during adolescence estimated from pandemic proportions infected, vaccinating schoolchildren would mitigate mortality among the very young and old more than vaccinating them. If within-group contacts predominated, to the limit implied by reproduction numbers < 3, infants would continue being better protected indirectly than directly, but the impact of these strategies among adults aged 65+ years become similar. Glasser and his collaborators assumed coverage and efficacy were independent of age, but insofar as access to health care or immune competence decline, the indirect strategy likely remains superior for elderly adults too. Their modeling suggests, paradoxically, that vulnerable people might best be protected by vaccinating schoolchildren. As neuraminidase inhibitors block viral replication, their timely medication also would minimize the requisite number or duration of treatments (i.e., selection for resistance), preserving those invaluable medications' effectiveness. While this work was centered on Taiwan, the methods are very relevant to Africa. The development of this work was influenced significantly by the opportunity to discuss it at the workshop and receive feedback from the participants.

#### Dynamics of HIV/AIDS: implications of antiretroviral treatment

Moatlhodi Kgosimore, Botswana College of Agriculture, Edward Lungu, University of Botswana, and Farai Nyabadza, University of Botswana, considered the dynamics of HIV/AIDS as individuals progress from an acute stage to the chronic stage, and ultimately to full blown AIDS. In their study, they investigated the benefits and consequences of universal and targeted treatment regimes. They derived conditions based on the reproduction number of the model under which the disease burden will be reduced. They further investigated consequences of treatment in terms of evolution of drug resistance, and benefits of treatment in terms of reduction in vertical transmission.

Structural determinants of variation in disease transmission

Justin Lessler, Johns Hopkins Bloomberg School of Public Health, and Derek Cummings, University of Pittsburgh, explored a new research area relating to the structural determinants of variation in disease

transmission. They took new mathematical and simulation based approaches to this problem. The observation that the majority of macro-parasitic infections are caused by a minority of cases has led to the crafting of the 20-80 rule, an expectation that the most infectious 20% of cases are responsible for 80% of transmission. More recently it has been suggested that this phenomenon also exists in micro-parasitic infections (e.g., the SARS super-spreader phenomenon). The existence of large heterogeneity in the transmissibility of individual cases has important implications for control programs as this characteristic may affect a pathogens ability to emerge in new settings, and point to particular individuals as targets for intervention. Lessler and Cummings showed that the 20-80 rule (or more generally the 20-XX rule where XX is large) is an intrinsic property of epidemic branching processes, deterministic or stochastic, in finite populations. They analyzed several epidemic models, and showed that heterogeneity in transmissibility of individuals is the norm even in models in which all individuals are identical due the dynamic impact of accumulated immunity. The expected proportion infected by the most infectious 20% is some larger percentage of the infectious individuals, the size of this proportion varying with the infectiousness of the disease. Using both compartmental and network based simulations, Lessler and Cummings assessed the effect of the basic reproduction number (a measure of the transmissibility of the pathogen), serial interval, contact network structure, and epidemic time on estimates of the 20/XX ratio. Another important factor to consider is the degree of susceptibility of contacts surrounding each individual at the time of his/her illness or as a proxy, the time or generation with the epidemic that an individual is infectious. This work suggests that rather than a Poisson distribution, a negative binomial distribution should be used to describe the expected variability in individual reproduction numbers due to stochastic effects in the absence of intrinsic variation between individuals in order to identify super-spreading vents. Recognizing the limitations of data describing the distribution of individual reproduction numbers aggregated over entire epidemics, Lessler and Cummings suggested procedures to identify heterogeneity individual transmissibility that is suggestive of intrinsic individual variation.

#### HIV in bisexual populations

Two of the student participants in the Johannesburg workshop, Evelyn Thomas and Ashley Crump were also accepted in the 2007 Advanced Study Institute. As part of the Institute they began projects which we fully expect to produce publications. Evelyn Thomas, Howard University, and her mentor, Abba Gumel, University of Manitoba, are modeling HIV in bisexual populations. The "down-low" effect is a term recently coined for the practice of covert bisexuality and/or homosexuality, specifically among African American males. Due to the social stigma of identifying with homosexual or bisexual orientations, these men engage in homosexual activity secretly while maintaining a heterosexual cover. There has been much anecdotal speculation as to the linkage of the "down low" to the HIV\AIDS crisis in the Black American community; however, the Centers for Disease Control and Prevention has never cited men on the downlow as the cause. Research in this area is limited due to the difficulty in identifying and gathering data on this particular community. Thomas and Gumel are developing a co-infection model of HIV and curable sexually transmitted diseases (namely gonorrhea). They will use this model to determine the measures that need to be taken to control these other diseases, which in turn will decrease the spread of HIV in this bisexually mixing population.

#### Pre-infection education effect on HIV

Ashley Crump, Howard University (another participant in the Johannesburg workshop who was accepted for the Advanced Study Institute), Anike Oliver, Howard University, and Zelalem Nigussa, University of Stellenbosch, together with their mentors Abba Gumel, University of Manitoba, and Edward Lungu, University of Botswana, are developing a model that will capture the effects of pre-infection education on transmission of HIV in a population. HIV has rapidly become a pandemic, affecting people from all parts of the world. Education may be one major factor that can control the spread of this disease. The model

includes age structure in the susceptible class. With this model, Crump, Oliver, Nigussa, Gumel, and Lungu hope to determine which age class in a population should be educated most in order to reduce the number of individuals with HIV in a given time period.

# **Training and Development**

One of the objectives of the workshop was to provide graduate students and junior researchers an opportunity to develop contacts with senior researchers and with students and junior researchers in Africa and North America. Below are comments from the participants on the success of the workshop.

"I would say that being in direct contact with an area that is so deeply and visibly affected by infectious diseases has reminded me to try to be practical in my research. That is, don't only study things to keep busy studying, but be sure that they could actually help the people you say you want to help. In the U.S., I think it's sometimes easy to lose sight of the goal and the impact that you ultimately want to have since most of us live in well-to-do areas and disease prevalence to us is sometimes nothing more than a statistic. It reminded me that it's important that what we study is not just interesting at an academic level, but that our work strives to comment on the current situation and furthermore, can enlighten health professionals or public health professionals as to how to improve upon it." Karyn Sutton, Ph.D. Student, Mathematics & Statistics, Arizona State University

"My participation led to my current PhD research work on HIV/AIDS at the Brunel University, UK. This research work has direct bearing to the immediate needs of the Africa." Nafiu Hussaini, Bayero University

"Attendance at the DIMACS Workshop: Facing the Challenge of Infectious Diseases in Africa: The Role of Mathematical Modeling led me and my colleague, Derek Cummings, to begin to explore a new research area relating to the structural determinants of variation in disease transmission. Some of the ideas presented in the conference gave us ideas for new mathematical and simulation based approaches to this problem. We are approaching the stage of writing the manuscript based on this work.

"As an epidemiology PhD student I also found benefit from the conference in meeting new potential collaborators both within the field and in mathematics. While these collaborations are in their infancy, I feel they show great promise." Justin Lessler, Johns Hopkins Bloomberg School of Public Health

"I just wanted to thank you again for giving me the opportunity to attend the workshop at Wits University. My visit there was very productive and more importantly, I came back filled with positive energy and deep desire to take part of the initiative of moving forward in supporting students from South Africa attain higher education." Miriam Nuno, Harvard School of Public Health.

"I would like to make some comments on the impact that the workshop on Facing the Challenge of Infectious Diseases in Africa had on me.

"As a result of this workshop, I had the opportunity to meet the faculty of the applied mathematics department at Witts University. Dr. Sherwell (chair of the applied maths program) expressed serious interest in having me join their applied math program and a day following the meeting I had the opportunity to spend a day in campus. To the current day, I have maintained contact with Dr. Sherwell and the invitation to join their department remains open. In addition to my contact with Dr. Sherwell I have maintained contact with other students that I met during my visit with this workshop.

"During this workshop I had the pleasure to meet Dr. John W. Glasser, a researcher at the CDC and share research interests. In addition to sharing my research ideas with Dr. Glasser, he invited me to submit my

job application to his research group and look into the possibility of getting a job position there. This workshop was instrumental in making this one-to-one connections that I know will strongly impact my opportunities in obtaining a job that fits my interests well. Finally, during this workshop I had the opportunity to engage more personally in several research and education related topics with Fred S. Roberts. I had met Dr. Roberts before this workshop, however, this workshop was particularly effective in promoting effective discussions. As a result of my interactions in this workshop I was recently invited to participate in BioMAP Epidemiology Module Writer's meeting that will be taking place in Boston during December 8-10 which I look forward to attend." Miriam Nuno, Harvard School of Public Health.

# **Outreach Activities**

Ashley Crump, one of the two undergraduates supported to attend the workshop, and the only undergraduate student accepted to attend the 2007 Advanced Study Institute, would like to reach out to other undergraduates and to high school students about her experiences in these programs.

# Books

# Papers

J. Glasser, D. Taneri, W. Thompson, J.-H. Chuang, J. Wu, P. Tüll, and J. Alexander, "Evaluation of targeted influenza vaccination strategies via population modeling," in clearance.

M. Kgosimore, A. Gumel, and E. Elbasha, "Modelling the epidemiological impact of viral loaddependent ART on HIV dynamics," work on progress.

M. Kgosimore, D.P. Clemence, M. Chen, and K. Herman, "Modelling the dynamics of HIV-TB coinfection in a population," work on progress.

M. Kgosimore, E.M. Lungu, and F. Nyabadza, "Public health models for implementation of ARV treatment," work on progress.

M. Kgosimore, J.Y.T. Mugisha, and R. Ouifki, "Models of vertical transmission of HIV/AIDS," work on progress.

J. Lessler and D. Cummings, "Structural determinants of variation in disease transmission," in preparation.

B.M. Moussa, A.D. Ciss, O.A. Koita, A. Tounkara, and D.J. Krostad, "Study of Glucose 6-phosphate dehydrogenase deficiency in Bamako population (Mali)," submitted.

A. Sissako, R.A. Diarra, O.H. Ciss, A. Coulibaly, H. Dembel, S. Mangara, L. Sangar, M. Sanogo, M.W. Bagayoko, T. Caudle, I. Mahamadou, M. Ciss, M. Suzanne, M. Keita, S. Siby, O. Koita and D.J. Krogstad, "Strategies to estimate the prevalence of CQ-resistant P. falciparum parasites," submitted.

# Talks

M. Kgosimore, E.M. Lungu, and F. Nyabadza, "Dynamics of HIV/AIDS: Implications of Antiretroviral Treatment," AMMSI Mathematical Biology Workshop 2006, Nairobi, Kenya, December 7-10, 2006.

M. Kgosimore, E.M. Lungu, and F. Nyabadza, "Dynamics of HIV/AIDS: Implications of Antiretroviral Treatment," Biomathematics Conference 2007, January 23 -26, 2007, Cape Town, South Africa.

F. Roberts, "Graph-theoretical Problems Arising from Defending Against Bioterrorism and Controlling the Spread of Fires," Talk at DHS Center for Dynamic Data Analysis program on Mathematics and Homeland Security for High School Teachers, May 2007

F. Roberts, "Applications of Measurement Theory/Meaningfulness in Epidemiology/Public Health," Plenary talk at European Mathematical Psychology Group meeting, Luxembourg, September 2007.

### **Other Specific Products**

# Reports

Claire Geoghegan, University of Pretoria and Carel D. Pretorius, SACEMA, "Facing the Challenge of Infectious Diseases in Africa, the Role of Mathematical Modelling," January 2007.

### **Group Discussion Reports:**

Carel Pretorius, SACEMA, "Epidemiology in Africa and its Unique Challenges for the Modeler."

Daniel Westreich, University of North Carolina at Chapel Hill, "Mathematical Modelling of Diseases with a Particular Burden on Africa."

Evelyn Thomas, Howard University, "Modelling Issues Arising from the Threat of Emerging Diseases in Resource-Poor Nations."

Nicole Ramsey, Howard University, "Optimizing the Use of Scarce Public Health Resources Discussion Group."

Miriam Nuño, Harvard University, "Professional and Mid-Career Development, Workforce and Collaboration Discussion Group Report."

# Web pages

# http://dimacs.rutgers.edu/Workshops/Diseases/

Main web page for DIMACS Workshop on Facing the Challenge of Infectious Diseases in Africa: The Role of Mathematical Modeling

# http://dimacs.rutgers.edu/Workshops/AIMS/

Main web page for US-Africa Advanced Study Institute on Mathematical Modeling of Infectious Diseases in Africa

#### http://dimacs.rutgers.edu/Workshops/AfricaDiseases/

Main web page for DIMACS Workshop on Mathematical Modeling of Infectious Diseases in Africa

# **Contributions**

# **Contributions within Discipline**

The discipline of mathematical epidemiology uses mathematical models to understand the spread and control of disease. We have initiated numerous collaborations between modelers and those who understand epidemiology, both at the faculty level and at the student level.

One of our goals has been to introduce U.S. modelers and future leaders in mathematical epidemiology to the specific issues facing modeling of infectious diseases in Africa. The partnerships formed among U.S. and African students and between U.S. and African faculty have already succeeded in achieving this goal. Here are some of the comments we received from participants in our Johannesburg program.

"Africa is the worst hit with the HIV pandemic. Modeling HIV with a view to providing guidelines to our health planners is vitally important. There are very few individuals working in HIV modeling in Sub-Sahara Africa. Indeed I lead the biggest modeling group consisting of three senior colleagues, four PhD students and seven masters students. I embarked on PhD and Masters training in 1996. So far, I have trained all the individuals working in this area.

"The DIMACS conference was extremely important to me because if we are to avoid inbreeding members of my modeling group should be exposed to other modelers and that is what the DIMACS conference provided to us, an opportunity to meet researchers from the USA. The interaction the conference provided was so vital to us. The contacts we have made since the conference has enhanced our work. Through that meeting, we made contact with individuals who have been able to send reading material to us. I have given email addresses to my PhD students who are now taking advantage of senior researchers in the USA and Canada. The DIMACS conference has made the burden of supervising lighter for me.

"I was particularly pleased with the comments US researchers made on our work namely how it can be improved and how it can be extended. We are holding a conference in Nairobi, Kenya and I am pleased that Prof Abba Gumel will be one of the resource persons. Prof Gumel has been very active in promoting disease modeling in Africa. He has been a source of inspiration to our researchers. It is through the DIMACS conference that we met Prof Gumel.

"Although the conference was held in September, a number of initiatives have started in our region. Our paper on modeling malaria has just been completed after the comments we received. The malaria paper was a poster presentation. Our paper on HIV and its mutation is about to be completed. Moreover, our PhD students are now working on problems that were suggested at the conference.

Overall, we have benefited a lot from attendance of the conference. We thank DIMACS for the opportunity." Edward Lungu, University of Botswana

"The Johannesburg workshop was a valuable opportunity to interact with young African and American graduate students and researchers. More such activities that allow for training African scientists are desperately needed and American researchers have a lot to learn during the course of these interactions. The most important of these lessons is in what questions to go after - often our work here is divorced from needs on the ground and from the African side - there is often lack of exposure to cutting-edge questions are being pursued in universities here. I hope you'll do more of these and would strongly suggest getting in touch with the Swedish SIDA for possible supplementary funding." Ramanan Laxminarayan, Resources for the Future

"The conference was a wonderful opportunity. Although the conference did not lead to any direct collaborations or papers at this time, it has definitely shaped my thinking and help focus my research. In addition to mathematical epidemiology, I am also focused on sustainability issues and modeling urban growth. This may have particular relevance to developing countries as we try to find new paradigms that

will lead to economic and urban growth that does not have adverse impacts on the environment. I have spoken about this trip to undergraduates during a class presentation to help motivate students to participate in research and graduate education. It sparked a lot of curiosity and debate concerning the opportunities in post baccalaureate education and what it means to do research." David Murillo, Arkansas State University

"As equally competent people were modeling influenza, I had until recently modeled other vaccinepreventable diseases. But health authorities in Taiwan asked me to model influenza. An invitation to this workshop afforded an opportunity for me to present to several fine mathematicians who are more knowledgeable about influenza.

"The Taiwanese wish to use vaccine that will be scarce everywhere, but especially near the source of the mutation or re-assortment that facilitates transmission person-to-person. The motivation of resource-poor African countries differs, but their problem will be the same. We developed a means of identifying sub-populations to target, thereby using this scarce resource most efficiently. A manuscript has been cleared externally and is in internal CDC clearance." John W. Glasser, CDC

"The workshop gave me another perspective of mathematics. The bond between Maths and Biology is obviously a necessary tool for the development of Science. Promoting collaborations between Mathematicians and Biologists must be a priority today. The fascinating thing about this workshop is the way it brought together Biologists and Mathematicians to deliberate on the same issue of fighting infectious diseases. This DIMACS workshop also gave me the opportunity to meet researchers from Africa and USA and exchange ideas with them." Mahamadou Ibrah, University of Bamako, Mali

"From a research perspective, this workshop initiated and enhanced already existing collaborations on topics that were discussed during this workshop. In particular, my work in collaboration with Dr. Chowell and Dr. Gumel that was presented during this workshop entitled "Assessing the role of basic control measures, antivirals, and vaccinein curtailing pandemic influenza: scenarios for the US, UK and the Netherlands" was recently accepted for publication in the Journal of the Royal Society Interface. I strongly believe that my presentation of this work at this workshop and the feedback that I received from the researchers there tremendously improved our work in this manuscript.

Dr. Gumel and myself also discussed further research ideas in modeling the impact of mother to child HIV transmission and the role of breast-feeding. Our discussions that resulted from attending this meeting are in the early stages of what will become a manuscript on this topic. In addition, this workshop enhanced my professional and research relationship with my collaborations Dr. Gumel and Dr. Chowell and as a result, we are currently carrying out further research projects that we hope to publish in the months to come.

Overall, this workshop co-organized by DIMACS and Witts University has enhanced my experience in research and has nurtured future collaborations. In particular, I am truly delighted with the numerous opportunities (career development and research) that have resulted from my attendance to this workshop." Miriam Nuno, Harvard School of Public Health

#### **Contributions to Other Disciplines**

This was a cross disciplinary project. The researchers and students at the workshop came from Biology, Biomathematics, Biomedical Engineering, Ecology, and Epidemiology as well as Computational Science, Computer Science, Mathematics, Physics, Statistics, and Public Health. The presentations and posters covered biology, mathematics, and economics as applied to the mathematical modeling of the spread and impact of infectious diseases.

### **Contributions beyond Science and Engineering**

A strong theme of the workshop was the use of the results of mathematical modeling by public health officials. Several participants commented on this. Here is one example.

"One of the most interesting issues arising out of the workshop was raised by Professor John Hargrove, who pointed out that all the modeling was theoretical and that what we really needed was models which demonstrated the workings of the real thing. I had been talking about archaic models of epidemics and the possibility of social disorganization from the conjoined epidemic of tuberculosis and HIV/AIDS. Since then I have looked back to my experience in tuberculosis control in Zimbabwe in the 1960s and early 1970s. I have also been following the interesting statistics from India where the ratio of male to female births has been changed rapidly and radically by ultrasound and gender based abortion. Simultaneously a major report on adult mortality has been published - masterminded by Barbara Anderson from the University of Michigan and Heston Phillips who works for Statistics South Africa. It shows dramatic demographic impact of communicable disease mortality skewed against young women. All this is by way of saying that doing the maths is a vital component of strategic planning." John Davies, University of the Witwatersrand

### **Contributions to Human Resources Development**

We expect that one of the outcomes of this project will be the incorporation of material specific to infectious diseases in Africa in the course material of the faculty participants. We also expect that participation in this project will have a profound effect on the future teaching of the students. Below is a sample comment.

"The Workshop on Facing the Challenges of Infectious Diseases in Africa: The role of Mathematical modelling, Johannesburg, South Africa, 2006 has contributed enormously to my personal development as a young Mathematical Modeller of infectious diseases in Africa. This would be extended to benefit the upcoming Mathematical Modelling students and/or other researchers in Botswana, America as well as in Africa in general.

My participation in the program has helped me a lot in career (review of journal articles), course development and advising students (University of Botswana postgraduate students). I have been involved in the development of Mathematical Epidemiology lecture notes (Lungu, Kgosimore and Nyabadza) for the US-Africa Advanced Studies Institute on Mathematical Modelling of infectious diseases in Africa (scheduled for 11 - 22 June 2007, at AIMS, Cape Town, South Africa). In my view, the goal of this program to increase international collaborations has been achieved; however a support structure needs to be put in place to support short visits and consultative meetings." Moatlhodi Kgosimore, Botswana College of Agriculture

At the Johannesburg meeting, there was a lot of discussion of "pipeline" issues of how to get more bright young people to go to graduate school rather than look for jobs. We were surprised to find that the notion of undergraduate research, and more specifically REU, was not really known among the Africans. Several of them expressed enthusiasm to learn from us how to put on REU programs. In particular, our hosts at Wits University were very interested in participating in one of the DIMACS REU programs and in taking ideas back to their own institution, possibly hosting U.S. students to collaborate in an REU program there.