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RE: Application to Mathematical Modeling of Infectious Diseases workshop

Background

I am currently in my 4th year of graduate studies in the AIM (Applied Interdisciplinary Mathematics) program at the University of Michigan. The AIM program is unique in that it encourages interdisciplinary work that connects mathematics with other disciplines. Students are required to take classes both in mathematics and a partner discipline, and with advisors both inside and outside of the math, work on a project that combines mathematics with an area of student's interest. On the mathematics side, I have taken a wide range of courses ranging from differential equations to probability theory and statistics. This has enabled me to build a sound mathematical base, providing me with a range of mathematical tools that I can apply with rigor and sophistication. I have taken up evolutionary biology as the field to integrate my mathematical interest. I am interested in modeling of infectious disease, and in particular the evolution of pathogen in regards to various attributes of disease caused by the pathogen.

Current Research and open questions

The project that I am currently working on focuses on disease caused by *Bordetellae* pathogens. This bacterial pathogen is known to cause “whooping cough” in children all over the world. *Bordetella* is also common in a range of mammalian host, causing diseases such as atrophic rhinitis in pigs and kennel cough in dogs. Interestingly, though, the species that is prevalent in humans, *B. pertussis* seems to have evolved from *B. bronchiseptica*-like ancestor, the species that is found in mammals. Furthermore, the two disease caused by the different species of *Bordetella* differ significantly in the pathogenesis and the course of infection. *Pertussis* infections in humans are more acute possibly resulting in high transmission, whereas, *Bronchiseptica* in mammalian hosts are less acute but persistent, usually indefinitely in the nasal cavity of the hosts. This raises the question of how the pathogen evolved over time, and what forces shape the evolutionary path for these pathogens.

Towards this, I am working with my advisor, Aaron King, to construct a framework that enables us to examine this question. In particular, we are interested in formulating mathematical models that captures the dynamics within a host and integrating that with a population level model. Early explorations seem to indicate that population level constraints might have played part in creating a niche for *B. pertussis*-like pathogen to successfully specialize a host. But there are several factors upon which the result of the model hinges on. One, for instance, is the dynamics with a host between the pathogen and the host immune system. Due to differential expression of genetic components that interact with host immune system in the two species of *Bordetellae*, the two diseases show vastly different infection. Capturing the mechanisms underlying the within-host

dynamics is one of the goal that I am working towards. The other component of the framework is exploring the spread of the disease in a given population structure. I am interested in examining how population level constraints are formed by differences in spatial structure of the population.

Why Advanced Study Institute

The workshop on Mathematical Modeling of Infectious Diseases at the Advanced Study Institute will provide me with a wonderful opportunity to learn about a wide range of topics in relation to understanding and modeling infectious diseases. My interest in infectious disease has grown as I have worked on the *Bordetella* project. Having only started working with infectious disease recently, most of the biology and epidemiology is relatively new to me. As I have begin to scratch the surface, the incredible complexity in the way pathogens interact with host immune system has fascinated me. Much more needs to be done in improving the model we have started working on. At this juncture, I feel the need to enhance my knowledge of infectious disease. As I venture into understanding the immunology behind it, and the modeling techniques that one can explore, a workshop of this kind would provide me with a larger perspective on these issues. I intend to interact with other student participants and leading researchers in various areas of disease modeling. The exposure I would get by closely working with students and researchers would be invaluable both in improving my research, and opening doors to further research opportunities.

Apart from the intellectual challenge, infectious diseases are a major cause of mortality and human suffering. Having born and grown up in Nepal, I am well aware of the public health concerns in poverty-stricken part of the world. I also maintain interest in working with epidemiologists and public health policy makers in understanding disease, and developing methods to tackle problems at a larger level. I believe that this workshop will give me a larger perspective that I am lacking.

I am committed to the project on *Bordetella* infections when I return back to Michigan upon completion of the workshop. The thesis project, I hope, will only be the first step for me in infectious disease modeling and research and will lead to many more research in future.