US-Africa Advanced Studies Institute on Mathematical Modeling of Infectious Diseases in Africa

Statement of Interest and Commitment

Background

At the beginning of my undergraduate career at Princeton, I intended to major in math and took several theoretical math courses. After three semesters I decided to major in Ecology and Evolutionary Biology with a focus on animal behavior. I continued to take several math courses, but directed my attention towards applied math. These courses included Advanced Multivariable Calculus, Biological Modeling, and Introduction to Biostatistics. During the summers after my freshman and sophomore I worked as a field research assistant on a California native bee ecology project and a radio telemetry project on periodical cicada dispersal in New Jersey, respectively. The following summer I conducted my senior thesis research on fiddler crab (*Uca terpsichores*) reproductive behavioral ecology in collaboration with the Smithsonian Tropical Research Institute in Panama. This research demonstrated that males of this species exhibit mate choice.

My interest in parasites, diseases, and epidemiology began while studying abroad at James Cook University in Townsville, Australia, the first semester of my junior year. I became interested in an emerging fungal parasite's (*Batrachochytrium dendrobatidis*) dramatic influence on amphibian diversity and abundance worldwide. The fungus produces free-living zoospores that cause chytridiomycosis, an often fatal disease, when they infect amphibians via transmission from streams, puddles, or other environmental reservoirs. The propensity of a free-living parasite to contaminate habitats and drastically alter community dynamics particularly fascinated me. When I returned to Princeton I attended a course on the ecology and epidemiology of parasites to learn more about infectious diseases. As an independent project I formulated a simulation model investigating how effects from competition with the highly invasive cane toad (*Bufo marinus*), chytridiomycosis, and interactions between the disease and invasive species (apparent competition) affect populations of native amphibians in tropical Australia. I realized that quantitative simulations can be a useful epidemiological tool for exploring various assumptions about disease dynamics and can also offer management implications. I decided that my quantitative and behavioral experience would be a valuable asset in increasingly interdisciplinary disease research projects and chose to immediately pursue this line of study in graduate school.

During my first year of graduate study at UC Berkeley's Department of Environmental Science, Policy & Management (ESPM), I have immersed myself in an ongoing program of anthrax research in Etosha National Park (ENP), Namibia (see Research Interests), under the guidance of my advisor, Wayne Getz. To gain the skills necessary to successfully develop empirical and theoretical research on anthrax epidemiology I have focused my coursework on wildlife ecology, statistics, and quantitative modeling. Last semester (fall 2006) I attended a course on spatial statistics and began a spatiotemporal clustering analysis[1] of long-term mortality data records kept by the Etosha Ecological Institute in ENP. This semester I am taking several public health courses (including Epidemiology and Control of Diseases and Modeling Infectious

Disease Processes). I intend to complete a MS in the UC Berkeley Division of Public Health jointly with my PhD in ESPM.

Research Interests

Anthrax is an important mammalian disease with global effects on human health, livestock management, and wildlife conservation[2]. Susceptible hosts become infected when they inhale, ingest, or expose a cutaneous lesion to spores of *Bacillus anthracis*, the causal bacterial agent of anthrax, though ingestion is the primary route of infection for wild and domestic animals[2,3]. Once inside a host, spores germinate into rapidly reproducing vegetative cells and produce a toxin, killing the host within days. Upon host mortality, terminal hemorrhaging exposes vegetative *B. anthracis* cells in host blood to oxygen, causing the sporulation of hardy, long-lasting spores[2,4]. Spores are capable of withstanding a wide range of environmental conditions and may survive for decades[2].

ENP is a 22,915 km^2 reserve in northern Namibia with high mammalian diversity, including a number of threatened and endangered species. In ENP, anthrax outbreaks occur during the wet season in three species of plains ungulates, Burchell's zebra (*Equus burchelli*), blue wildebeest (*Connochaetes taurinus*), and springbok (*Antidorcas marsupialsi*), and during the dry season in elephants (*Loxodanta africanus*)[4]. ENP exhibits annual outbreaks but does not manage the disease, providing an ideal research site for studying anthrax ecology in a natural environment.

I am particularly interested in how scavengers may affect disease dynamics by consuming infectious material at carcasses. While fatal septicemia and terminal hemorrhaging in infected mammalian hosts combine to expose vegetative cells in host blood to oxygen, scavengers—while immune to anthrax in ENP—may further stimulate additional sporulation by opening and moving carcasses. Evidence also suggests that sporulation may continue for up to two days after host death. Thus, scavengers may also "sanitize" carcass sites by consuming vegetative bacteria before they sporulate[4]. While lacking empirical justification, speculative debate regarding this tradeoff has motivated management approaches[2,5] and therefore warrants attention in the form of experimental field research and quantitative modeling.

Scavengers also disperse *B. anthracis* spores in the environment via consumption of spore-laden material and subsequent defecation[4]. The importance of spore-contaminated feces in outbreak generation also remains poorly understood. Generally, little is known concerning the spatial distribution of *B. anthracis* spores throughout the park. Previous research indicates that anthrax-positive carcass sites often exhibit infectious spore concentrations months after the host's death, but systematic soil and water samples throughout the park have not exhibited any significant spore concentration. This suggests that contaminated areas may be of a small spatial scale but high concentration (e.g. localized infectious zones (LIZs)). I intend to assess carcass sites and areas containing high densities of scavenger scat as potential LIZs.

While many microbiological aspects of *B. anthracis* virulence have been extensively studied[2], a better understanding of anthrax epidemiology requires more empirical and theoretical focus on anthrax ecology in the environment. Several characteristics of anthrax ecology particularly present challenges for empirical and theoretical research. First, unlike many infectious diseases anthrax transmission is not direct (host to host) or vector-borne, but rather occurs via exposure to an environmental reservoir (like cholera and chytriodiomycosis). Thus, identification of factors leading to sporadic anthrax cases, episodic outbreaks, or periodic epidemics requires assessment of the spatial and temporal distributions of *B. anthracis* spores. However, the scale of susceptible host movement and the scales of spore distribution are hardly comparable. Systematic sampling for spores in the environment can easily degenerate into "looking for a needle in a haystack". Second, hosts die days after anthrax infection, making identification of live and infected hosts difficult. This prevents any research into how infected hosts' movement patterns reflect the location or time of their exposure. Finally, recent laboratory studies demonstrate *B. anthracis* spores' ability to germinate in association with plant roots[6], suggesting small spore concentrations may amplify over time under appropriate conditions. Until we understand if and when small concentrations of spores amply to infectious levels and the dynamics of spore concentration from year to year, snapshot sampling of environmental spore concentrations may support misleading conclusions regarding the spatial distribution of spores.

To understand anthrax ecology in the environment requires a combination of long-term field research and hypothesis-generating dynamic models that account for host behavior and exposure, initial spore production upon host death, and subsequent patterns of spore dispersal, persistence, or amplification. An appropriate dynamic model will also account for the multiple scales of anthrax ecology and will be relevant to other free-living or sporulating pathogens. I am intrigued by the challenge to integrate animal behavior and environmental anthrax ecology into a coherent dynamic model.

Future Plans

During my graduate career at UC Berkeley, I will focus my research on field studies and theoretical modeling of anthrax ecology and scavenger behavior in ENP. I am also interested in using simulated data to compare the sensitivity and specificity of various statistical methods to detect the spatial or temporal scales of disease dynamics. This summer I will begin my field research in ENP. I will acquaint myself with the park's geography, staff, management, and anthrax incidence and also conduct pilot research on my field methods. The Advanced Studies Institute workshop would provide a fantastic opportunity to improve my modeling skills and establish a variety of contacts from the US and Africa for future collaboration on my ENP research and further on in my career.

Eventually, I plan to teach as a university professor. I also intend to continue to research and to participate in infectious disease policy discussions. As a joint PhD/MPH student at UC Berkeley I intend to develop interdisciplinary skills for researching, modeling, and managing infectious diseases. Diverse faculty expertise in applied mathematics, environmental science and policy, infectious diseases and biology will help me attain this goal. Additionally, I will prepare for a career in education by working as a graduate student instructor in courses relevant to my field of study.

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