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CAREER: Dynamics of Hierarchical HouseholdStructured Epidemiological Models

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Preview of Award 0746603 - Final Project Report

Cover

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Signature of Submitting Official (signature shall be submitted in accordance with agency specific instructions)	David Hiebeler

Accomplishments

* What are the major goals of the project?

1. Use moment-closure techniques to develop models of infectious diseases spreading through community-structured populations.

Specific types of models to be studied include:

2. Treatment efforts targeted at more highly-infected communities

3. Clustered resistance/vaccination distributions among communities

4. Temporally varying, spatially structured resistance

5. Application of the models to studying the spread of malicious software ("worms") through computer networks

*** What was accomplished under these goals (you must provide information for at least one of the 4 categories below)?**

Major Activities: Development of techniques capable of simulating the spread of an infectious outbreak through a hierarchically-structured population of 4.3 billion individuals, at reasonable speeds on a desktop computer or even an iPad. This enables us to simulate the spread of malicious software through the entire Internet.

Specific Objectives: ====

Significant Results: Community-structured models with clustered vaccination:

An algorithm to generate a distribution of vaccination levels among communities was developed, to facilitate studying the spread of infections in populations with heterogeneous vaccination levels.

One surprising result from the model is that increasing the efficacy of a vaccine, i.e., decreasing the chances that a vaccinated individual will become infected when contacting an infectious individual, can actually *increase* the initial rate of spread of an infection once it arises within a population. This occurs when the infection is introduced by repeated reintroductions into the population from outside until someone becomes infected (becoming "patient zero"). As vaccine efficacy increases, it takes longer for an infection to begin within the population under consideration, but the heterogeneity in herd immunity among the communities increases the chances that the infectious outbreak begins within a less-vaccinated community. This causes the infection to spread more quickly from that initial location, and can outweigh the decreased rate of spread due to the higher efficacy of the vaccine.

The dominant eigenvalue for a next-generation operator describing the spread of an infection within one "generation" gives the rate of spread after the initial conditions are no longer playing a significant role, but before the infection has become prevalent enough to slow down due to density dependence. Our model shows that the dominant eigenvalue comes close to matching the "worst-case scenario", where the outbreak begins spreading from the least-vaccinated community in the entire population. This again emphasizes the need to not only vaccinate a significant proportion of the population, but to ensure that there are no significant "hot spots" where vaccination levels are especially low.

The location in which an infection begins was shown to have a large impact on the likelihood that the infection spreads to a significant portion of the population (and its initial rate of spread), but relatively little influence on the actual final outbreak size.

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Heterogeneous parameters

The model was also explored using fixed heterogeneous parameters, such as varying recovery rates among communities. We found that increasing the variability in recovery rates increases equilibrium infection levels; the strength of this effect depends on the prevalence of global interactions in the population. With primarily localized infections, there is a threshold effect, where infection level only begins to rise after inter-community variances passes a critical value.

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Targeted treatment

Dynamic heterogeneous parameters were also studied, where treatment may be more focused on communities with higher infection levels to better control outbreaks. Two versions of the model were considered, where treatment was either "passive" (e.g., aerial spraying of agricultural fields to treat crops infested by an invasive species, where healthy plants within the field are also sprayed) or "active" (where only infectious individuals receive treatment).

In some cases, targeted treatment makes things much worse: outbreaks are more likely to occur, spread more quickly, and reach higher levels, compared with simple homogeneous treatments. This is because of how targeted treatment affects the inter-community variance of infection levels, but it can be simply understood by noting that an infectious individual in an otherwise-healthy community can do much more damage (quickly infect more individuals) than it could in a highly-infected community, where much of its contact would be with already-infected individuals and therefore have no effect.

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Moment-based approach to community models

We also explored the effects of two types of variability within community-structured models: variability among communities within a population, and stochastic variability between populations or realizations of the process. A previous version of this model neglected the second type of variability. The improved model consisted of a system of ordinary differential equations describing the moments of the probability distribution of infection levels among the communities. We found that introducing this variability into the model produced numerical instabilities in solutions to the ODEs. Reparameterization methods used in the earlier version of the model were no longer successful. We finally found an alternative characterization of the system which did not suffer from these instabilities.

Our model explicitly included finite population size, unlike the simplified model which assumed infinite population size. In theory, this allows our model to be applicable even for small population sizes. In practice, however, the moment-closure approximations suffered greater inaccuracy when the population size was small, suggesting that other approaches (such as branching processes) may still be best for very small population sizes.

The stark difference in behaviors of the model depending on which representation we used was a large source of frustration, but our eventual discovery of a way around the problem will hopefully help inform development of the many additional models we are building based on this work.

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Internet worms

The community-structured population models were applied to studying the spread of malicious software ("computer worms") through the Internet. We run our simulations on simulated Internets with the mean and variance in susceptibility levels calibrated based on scans of the actual Internet.

Our model shows that the existing computer worms such as Code Red II were able to spread much more efficiently than they could using simple random scanning. More localized dispersal strategies in worms can increase the average rate of spread, though with increased variability in spread rates (i.e., high-risk high-reward).

Some worms use adaptive strategies, where the amount of effort they dedicate to dispersal at various spatial scales is affected by how successful they are at spreading. We found that such strategies can be even more effective, but we have not yet seen a worm which fully exploits the benefits of such a strategy. Our predictions are that we will someday see a worm which uses actual evolution of parameters to spread more efficiently. Frankly, we are surprised such as worm has not been seen already.

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Heterogeneous habitat with continuous-valued habitat quality

Methods from the community-structured population models were applied to a well-mixed population model, with continuous-valued heterogeneous habitat quality.

We observed habitat association in the model, where "Occupied Habitat Quality" (OHQ, the average quality of occupied sites) is larger than "Total Habitat Quality (THQ, the average quality of all sites). We also showed that this difference decreases as population density increases, when the population is being pushed into persisting on lower-quality sites. As in the epidemiological models, increasing the variability of the habitat quality of all sites in the landscape makes it easier for the population to persist.

We showed that observed differences in population densites between two species among individual sampled sites is not necessarily an indication of which species would be more successful in general, but may simply reflect the distributions of available habitat quality as perceived by the two species. It's possible for one species to have a lower population density for any given level of habitat quality, but a higher overall population density across an entire landscape due to the distributions of habitat quality. It's also possible for one landscape to have a lower average habitat quality (THQ) than a second landscape, but still have higher population density for the species of interest, due to differences in the variances of habitat quality in the two landscapes being compared.

Key outcomes or Other achievements:

*** What opportunities for training and professional development has the project provided?**

All of the various students (graduate students, undergraduates, and high-school students) gained software skills (C and Objective C programming languages, R and Matlab software platform, Apple XCode development environment) by working with the PI and/or more senior students on the project. Almost all of them also gained experience in working with differential equation models and stochastic processes.

*** How have the results been disseminated to communities of interest?**

In addition to providing free apps on Apple's iOS App Store and Google Play, numerous educational outreach workshops have been done with groups of K-12 students and teachers, and more are planned. Workshops are also currently being planned for a Maine Science Festival to be held in 2015. And we are in the final stages of installing two iPads in the Maine Discovery Museum for children, to allow children to do hands-on exploration with simulation models (while their parents hopefully learn that mathematics has wider applications to the natural sciences, and that immunizations against infectious diseases is crucial to control their spread).

Products

Books

Book Chapters

Conference Papers and Presentations

Inventions

Journals

David E. Hiebeler, Rachel M. Rier, Josh Audibert, Phillip J. LeClair, and Anna Webber (2015). Variability in a Community-Structured SIS Epidemiological Model. *Bulletin of Mathematical Biology*. . Status = PUBLISHED; Acknowledgment of Federal Support = Yes ; Peer Reviewed = Yes

Licenses

Other Products

Software or Netware.

An app ("SPEED Sim") for iPad/iPhone/iPod Touch, available for free on Apple's iOS store. A version for Android was also released on Google Play, but is no longer being actively maintained. This app is being used in educational outreach activities with various groups of K-12 students, and will be used in workshops in an upcoming Maine Science Festival.

Other Publications

Patents

Technologies or Techniques

Thesis/Dissertations

Websites

Participants/Organizations

What individuals have worked on the project?

Name	Most Senior Project Role	Nearest Person Month Worked
Hiebeler, David	PD/PI	4
Cangelosi, John	K-12 Teacher	0
Rode, Sonia	Graduate Student (research assistant)	4
Buchak, Timothy	Undergraduate Student	0
Dunn, Nathan	Undergraduate Student	0
Audibert, Josh	High School Student	0
LeClaire, Phillip	High School Student	2
Webber, Anna	High School Student	2

Full details of individuals who have worked on the project:

David Hiebeler
Email: hiebeler@math.umaine.edu
Most Senior Project Role: PD/PI
Nearest Person Month Worked: 4

Contribution to the Project: Developing primary research techniques; overseeing graduate students, undergraduates, and high-school students working on the projects.

Funding Support: N/A

International Collaboration: No
International Travel: No

John Cangelosi
Email: jcangelosi@bangorschools.net
Most Senior Project Role: K-12 Teacher
Nearest Person Month Worked: 0

Contribution to the Project: Some help training the K-12 students, and evaluating their presentations of their work on the project.

Funding Support: N/A

International Collaboration: No
International Travel: No

Sonia Rode
Email: sonia.rode@maine.edu
Most Senior Project Role: Graduate Student (research assistant)
Nearest Person Month Worked: 4

Contribution to the Project: Helping develop educational outreach software (iOS and Android apps), and develop software for simulating the spread of malicious software through the Internet.

Funding Support: N/A

International Collaboration: No
International Travel: No

Timothy D Buchak
Email: krayterzoff219@gmail.com
Most Senior Project Role: Undergraduate Student
Nearest Person Month Worked: 0

Contribution to the Project: Analyzing differential equation models

Funding Support: None

International Collaboration: No
International Travel: No

Nathan Dunn
Email: Nathan_Dunn@umit.maine.edu
Most Senior Project Role: Undergraduate Student
Nearest Person Month Worked: 0

Contribution to the Project: Analyzing differential equation models

Funding Support: None

International Collaboration: No
International Travel: No

Josh Audibert
Email: jaudibert13@gmail.com
Most Senior Project Role: High School Student
Nearest Person Month Worked: 0

Contribution to the Project: Writing, running, and analyzing simulations

Funding Support: None

International Collaboration: No
International Travel: No

Phillip LeClaire
Email: peej65@gmail.com
Most Senior Project Role: High School Student
Nearest Person Month Worked: 2

Contribution to the Project: Writing, running, and analyzing simulations. Helping develop outreach software (iOS app).

Funding Support: None

International Collaboration: No
International Travel: No

Anna Webber
Email: agw429@gmail.com
Most Senior Project Role: High School Student
Nearest Person Month Worked: 2

Contribution to the Project: Assisting with writing, running, and analyzing simulations. Helping develop outreach software (iOS app).

Funding Support: None

International Collaboration: No
International Travel: No

What other organizations have been involved as partners?

Nothing to report.

What other collaborators or contacts have been involved?

NO

Impacts

What is the impact on the development of the principal discipline(s) of the project?

Exploration of various moment-closure approximations was done within the context of a hierarchically-structured population, to investigate the dynamics of within- and between-population variance during the spread of an infectious outbreak. Hopefully the characterization of the two types of variance within the framework of moment dynamics of epidemiological models will help other investigators studying stochastic epidemiological models.

What is the impact on other disciplines?

A basic software template in C to automate running simulations over a range of parameter values was made freely available. This software runs either on single-core computers, or on multi-core computers and clusters via OpenMPI.

What is the impact on the development of human resources?

Two high-school students gained fairly extensive experience with the C and Objective-C programming languages, and in programming iPad software via Apple's XCode development environment. They also participated in a K-12 outreach event, letting a group of high-school students do hands-on experimentation with simulation models on iPads.

What is the impact on physical resources that form infrastructure?
Nothing to report.

What is the impact on institutional resources that form infrastructure?
Nothing to report.

What is the impact on information resources that form infrastructure?
Nothing to report.

What is the impact on technology transfer?
Nothing to report.

What is the impact on society beyond science and technology?

Seeing how the spread of infectious diseases is enabled by "hot spots" (communities where an above-average proportion of individuals opt out of vaccionation, even where the population-wide vaccination level is high) may hopefully increase awareness of the dangers of choosing not to be vaccinated.

Changes/Problems

Changes in approach and reason for change
Nothing to report.

Actual or Anticipated problems or delays and actions or plans to resolve them
Nothing to report.

Changes that have a significant impact on expenditures
Nothing to report.

Significant changes in use or care of human subjects
Nothing to report.

Significant changes in use or care of vertebrate animals
Nothing to report.

Significant changes in use or care of biohazards
Nothing to report.

Special Requirements

Responses to any special reporting requirements specified in the award terms and conditions, as well as any award specific reporting requirements.
Nothing to report.