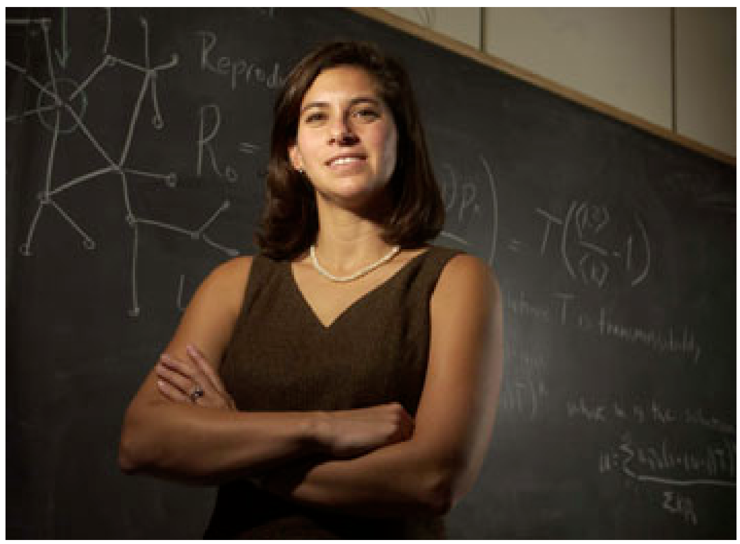
Predicting the Path of Infectious Diseases

Mathematical modeling traces the spread of SARS and other illnesses through human contact

When severe acute respiratory syndrome (SARS) arrived in the Canadian cities of Vancouver and Toronto last spring, its first cases looked remarkably similar. Both came from individuals who were infected at the Metropole Hotel in Hong Kong and then flew home to Canada. In Vancouver, however, no additional cases grew out of the initial infection. In Toronto, that single case sparked a huge outbreak where ultimately hundreds of people were infected. Why did such different scenarios grow out of nearly identical situations?



Dr. Lauren Ancel Meyers helps create mathematical models that not only predict the spread of disease but can also simulate various interventions strategies to determine the one that might be most effective.

"It sounds intuitive, but the key difference between these scenarios is that the infected individuals had very different contact patterns," says Dr. Lauren Ancel Meyers, an assistant professor of integrative biology at The University of Texas at Austin. "In the Vancouver case, the man lived alone with his wife, and he went immediately to a hospital where he was isolated and where caregivers took significant precautions while treating him. In the Toronto case, the woman was from a large multigenerational family. She died at home as an undiagnosed case of SARS, meanwhile exposing many people in her family who later went on to expose other people.

"So the contact patterns of the first few cases can make all the difference as to whether you get a big outbreak or epidemic or none at all."

Understanding the contact patterns in a community is central to Meyers' research. She uses mathematical modeling to track and predict the spread of infectious diseases in a community. Earlier this year the University of British Columbia Centre for Disease Control (UBC CDC) asked her to help them understand the spread of SARS in Canada and worldwide and to determine the most appropriate intervention strategies to stem the disease.

Meyers worked with Dr. Babak Pourbohloul, director of mathematical modeling at the UBC

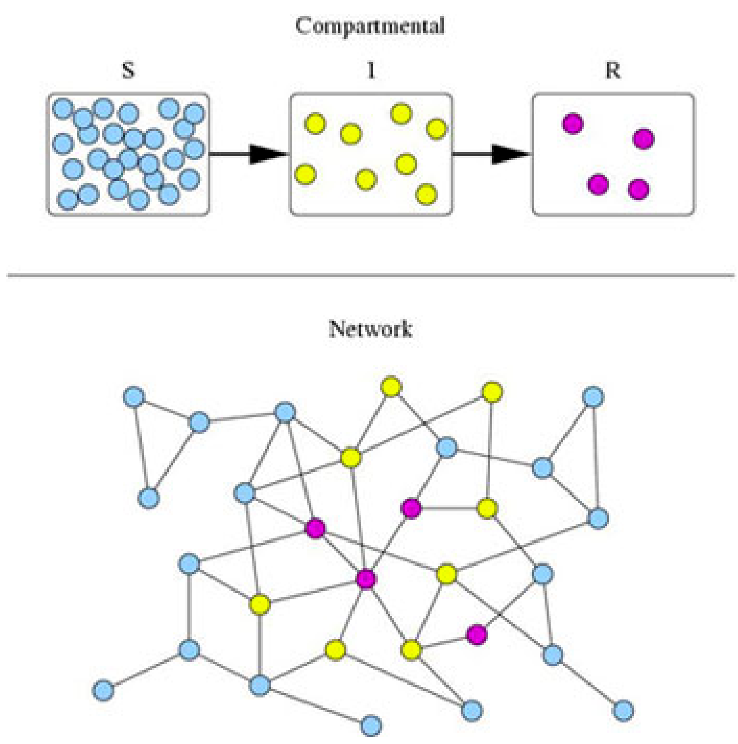
CDC, and members of the Scientific Investigators' Vaccine Initiative (SIVI) to create a mathematical model that describes the spread of SARS through a city. Using demographic and census data from Vancouver, they built a model of the patterns of interaction in the city. Household size, the number of houses, distribution of schools and hospitals and other data allowed them to construct a network that represents the way individuals actually interact in the community. Once they understand those interactions, they can predict how rapidly a disease will spread, what parts of the city are most at risk and what preventions are most effective in stopping it.

Using mathematical models to analyze the spread of the disease isn't new, but Meyers and other researchers are approaching modeling in a new way, using network theory.

In the past, most mathematical modeling of epidemics was undertaken by separating a population into three or more distinct groups: those who are susceptible to a disease, those who are already infected and those who have recovered. It assumed that there was some probability that those who are susceptible would come into contact with those who were infected, that those who were infected would recover, and that in some cases, those who recovered would once again become susceptible.

"This doesn't take into account the true heterogeneity of contact patterns that underlie the spread of disease," says Meyers.

In reality, all susceptible people do not face the same risk of contracting a disease. An elderly person living alone at home is much less likely to come into contact with an infected person than someone who works in a large office building or a hospital, for example. In the initial Canadian SARS cases, it is clear that living in a large family increased the chance of contracting a disease. The type and frequency of interactions that a person has with others is key to determining who may become infected.



Traditional mathematical modeling of epidemics (top) places individuals in large groups and tries to predict the probability of movement from one group to the next. Network theory (bottom) allows researchers to build more complex models that take into consideration the contact patterns of individuals.

"Using network theory, instead of grouping people into populations, we take into account every single person, and every single person becomes a point in a network," says Meyers. "Now let's say a person brings a disease like SARS into a community. We can predict what parts of the community—the network—will be infected, how quickly it will spread, and how best to stop it ."

Network theory is often used by researchers investigating social interactions, and it's become popularized in the past decade through the concept of "six degrees of separation." "Six degrees of separation" asserts that each person on the planet is at the most removed from every other person by six degrees, or six connections with others.

The term was popularized by the playwright John Guare, who wrote a play of the same name which was later made into a movie. And a few years ago some college students in Pennsylvania created a "six degrees of Kevin Bacon" game that become an instant fad, asking players to link the ubiquitous actor to other actors in a maximum of six steps.

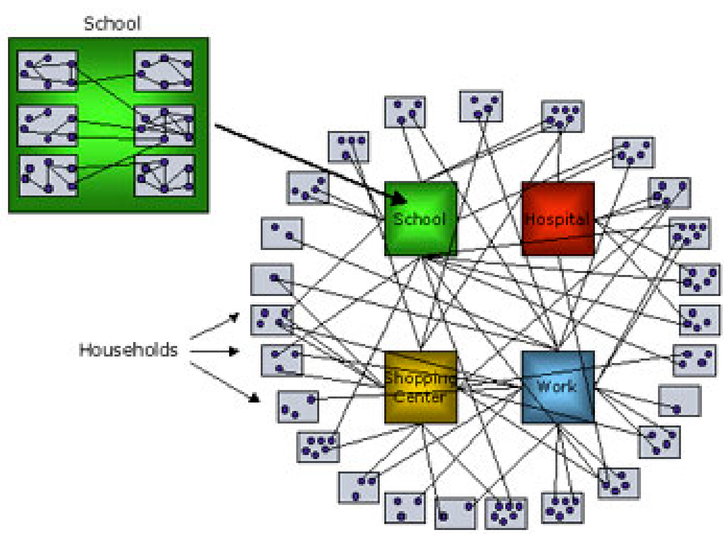
The mathematical models Meyers builds borrow from sociological approaches. The models account for the points of connection between individuals.

"Each person within a community is represented as a point in the network," Meyers explains. "The edges that connect a person to other people represent interactions that take place inside or outside of the home, including interactions that take place at school or work, while shopping or dining, while at a hospital, etc. The network thereby captures the diversity of human contacts that underlie the spread of disease."

Some people may come into contact with very few people, but others may have many strands connecting them to other people in the community through their work or social habits. If this person becomes sick, he or she has the potential to become what researchers call a "superspreader," someone who spreads disease to a lot of people in the community. Identifying potential superspreaders is one step in curbing an outbreak.

This type of mathematical modeling may have important implications for public health officials. When the SARS outbreak began, officials were in a quandary. They needed to act quickly to control the spread of the disease, yet they lacked the information necessary to determine which interventions would be most effective. Would they be best served by closing schools or by supplying health care workers with better face masks, by limiting air travel or by waiting for a vaccine? Such decisions may be easier to make in the future, thanks to advances in mathematical modeling.

"Mathematical models allow us to simulate the spread of diseases through different kinds of settings and test different kinds of interventions," says Meyers. "This can give policymakers the tools and confidence to make educated decisions."



This shows a municipal contact network. In a city, SARS can spread within households, schools, workplaces, hospitals and public spaces. The lines between the dots represent contacts between individuals that could potentially lead to disease transmission.

Meyers first started working on mathematical models in the spread of infectious diseases while doing post-doctoral research in Atlanta and at the Santa Fe Institute. She collaborated with Mark Newman from the University of Michigan, one of the pioneers of epidemiological network modeling, and some researchers at the Centers for Disease Control and Prevention (CDC) who were trying to figure out how to stop the spread of mycoplasma pneumonia—known as walking pneumonia—in hospital wards, military barracks, college campuses and other places where individuals come into close contact.

"Before we began this project, the CDC hadn't yet determined the best strategies for controlling the spread walking pneumonia because they can rarely do experiments when an outbreak is in progress," Meyers explains. "They can't treat half the population and not the other half. It is also difficult to compare the success of interventions on different outbreaks because the settings in which they take place are often quite distinct."

Meyers and her collaborators developed a mathematical model of a psychiatric institution in Indiana, building a network that accounted for everyone who works or lives in the facility. She found that while the focus is generally on preventing the spread of walking pneumonia from patient to patient, caregivers play a much more important role in the large-scale spread of respiratory infections across such a facility. Caregivers pick it up in one ward and spread it to the next, and because of their diverse patient load, a few infected caregivers can potentially lead to the infection hundreds of patients.

"Looking at this from a network modeling perspective allowed us to see how important changing the behavior of caregivers is to stopping an outbreak," Meyers says.

The models then enable researchers to simulate a change in caregiver behavior and project the response in the spread of disease. This allows policymakers to test possible interventions before investing time and money into them.

And should SARS or another respiratory-borne illness threaten Vancouver, policymakers there will similarly be able to test possible interventions before implementing them.

Because contact patterns differ from community to community, mathematical modeling requires that a model be built for each individual community. Meyers and Pourbohloul are currently working with a large team of Canadian epidemiologists and infectious disease experts to build network models of four Canadian hospitals and two communities—one rural and the other urban. Once good network models of these hospitals and communities are in place, they can be used to predict and control the spread of all kinds of diseases.

Air travel can enable illnesses like SARS and flu to cross international borders. Meyers is working on a model of global disease transmission based on flights in and out of American cities.

At the same time, modeling these distinct communities will allow researchers to look to see if they can draw any generalizations across communities. They hope to be able to say that, in general, one type of intervention works better than another. Ideally, however, each community, be it a large city like Toronto or a community like The University of Texas at Austin campus, would have its own model to use as a tool for preventing the spread of disease.

Meyers likes the idea of building some models closer to home, be it for Texas or Austin or the university campus. In the meantime, she's working on Canada and beginning to build a network model of global disease transmission based on the flights in and out of American cities. This kind of larger scale model would be extremely helpful for diseases like SARS and flu that cross international borders.

When reflecting on networks, Meyers calls to mind one of this year's other big news stories: the big power outage.

"You can think about electricity spreading along a grid like disease spreading through a population," she says. "But our goals for electricity and epidemiology are opposite. With electricity, you want to make sure your network is built so that if something happens to cut down one of your links, the whole system is not going to crash. In the case of disease, you want to break the connections through vaccinations or other interventions that most effectively stop its spread."

Vivé Griffith

Photos: **Marsha Miller**

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