have about the same number of lifetime sexual partners (and the same as for Western countries), but there are big differences in concurrency. After discovering this, Martina got governments and tribal leaders and anyone else who would listen to stigmatize the behavior, and it really seems to make a difference. There is a lot of substance hiding behind this paragraph, and their work is a thrilling success. Go take a look.

(2) The theorists had no idea how well developed the computational resources are. One had only to suggest a project, and someone could sit down in real time and try it out. STATNET and R are amazing.

(3) I don't think that the applied people had internalized some of the theoretical progress. Graph limit theory is full of infinite-dimensional analysis, and its main applications have been to extremal graph theory. After some of its potential applications (see below) were in believable focus, there was a lot of explaining and discussing. This was useful for me too.

(4) Here is a success story from the workshop. An exponential random graph model has an ÒunknowableÓ normalizing constant, which is a sum over all graphs on n nodes. Even for little graphs ($n = 30$) this is too big to handle with brute force. Chatterjee and Diaconis proved a large sample approximation for the normalizing constant. This was in terms of an infinite-dimensional calculus of variations problem, but sometimes it reduces to a one-dimensional optimization. Their approximation is based on large deviations bounds (due to Chatterjee and Varadhan). Its relevance to finite n could and should be questioned. Mark Handcock and David Hunter programmed the tractable approximations and compared them to Monte Carlo approximations that are well developed in the applied world. To everyone's amazement, the approximations were spot on—even for $n = 20$. These approximations have parameters in them and are used to compute maximum likelihood and Bayes estimates. If things work out, there are really new tools to use and develop.

Two questions had all of us interested. Once one realizes that this route is interesting, one can try to find approximations of the not-so-nice infinite-dimensional problems by discretizing. This is quite close to what physicists do in "replica symmetry breaking," so there are ideas to borrow and specific projects to try out. Second, some of the statistics that the applied community finds natural are not continuous in graph limit space. What does this mean in practice, and can the theorists come up with continuous functionals that are similarly useful.

There are a dozen other successes. Some small, some big. I think that all of us enlarged our worldview and made some useful new scientific friends.

Reference:

[1] László Lovász, *Large Networks and Graph Limits*, Colloquium Publications **60**, American Mathematical Society (AMS), Providence, Rhode Island (2012).

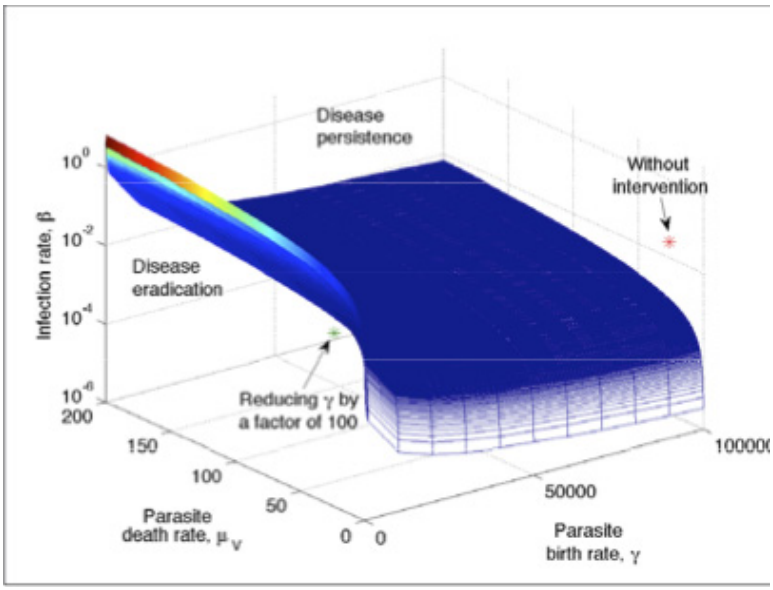
Contributor: Persi Diaconis

Posted: July 2, 2013

13.4 ▪ Using Mathematical Modeling to Eradicate Diseases

Guinea Worm Disease is a parasitic disease, spread via drinking water, that has been with us since antiquity. (It is mentioned in the Bible, and Egyptian mummies suffered from it.) Essentially, the parasite attaches itself to a water flea, you drink the flea, and your stomach acid dissolves the flea, leaving the parasite free to invade your body. Because of gravity, it usually makes its way to the foot, where it lives for an entire year.

After a year, your foot is burning and itching, so you put it in water. And if your village only has one source of water, then that source often ends up being the drinking



water. At this point, the fully grown worm bursts out of your foot, spraying forth 100,000 parasites and hence restarting the process.

Unfortunately, there is no drug to treat Guinea Worm Disease, and there is no vaccine either. Miraculously, however, Guinea Worm Disease is about to be eradicated, making it the first parasitic disease to be eradicated and the first to be eradicated without biomedical interventions. This is largely thanks to the efforts of former President Jimmy Carter. So how can one eradicate a disease without a drug, vaccine or immunity?

Using a mathematical model, we can quantify the major factors that we can control: education (reducing the parasite birth rate γ), filtration (reducing the transmission β) and chlorination (increasing the parasite death rate μ_V). The basic reproductive ratio R_0 represents the mean number of individuals infected by each infected individual. Hence, eradication starts under the threshold $R_0 = 1$.

The figure represents the level surface $R_0(\gamma, \beta, \mu_V) = 1$. If you are above the surface, then R_0 is greater than 1 and the disease will persist. If you are below the surface, then R_0 is less than 1 and the disease will be eradicated.

Increasing the parasite death rate involves moving along the μ_V axis to the rear left. But the level surface is very shallow, so you need to move a long way to the back corner to get under the surface. Reducing transmissibility involves moving down the β-axis. But this is on a log scale, so that takes much longer than it first appears. However, see how steep the surface is for small γ? This makes it very easy to move under it by a small change in γ. This suggests that eradication should occur if we stick to one strategy: reducing the parasite birth rate.

Encouraging people not to put their infected limbs in the drinking water means that each time a worm doesn't burst into the water and 100,000 parasites aren't released. What this means is that, in the final push to eradication, we should concentrate our efforts on reaching remote communities, informing them about the specifics of Guinea Worm Disease and its transmission cycle. Of course, a combination of all three factors will help. But it's education that holds the key to removing this ancient scourge and points the way forward to controlling or eradicating other diseases without waiting for someone to

develop a vaccine. If we can harness the power of education, we can change the world.

Contributor: Robert Smith?

Posted: September 12, 2012

13.5 ▪ Neglected Tropical Diseases – How Mathematics Can Help

You might have heard of a group of diseases called the “Neglected Tropical Diseases." This isn't just a generic title for all the forgotten diseases in the world; it's a specific designation on behalf of the World Health Organization for 13 particular diseases that qualify for neglected status. Collectively, these diseases infect about one sixth of the world's population.

The diseases in question include three types of worm (hookworm, roundworm and whipworm), a number of helminths (elephantitis, river blindness, Guinea worm disease, and schistosomiasis), protozoans (leishmaniasis, Chagas' Disease, sleeping sickness) and bacterial infections (the Buruli ulcer, leprosy and trachoma). Approximately 4.2 billion people—more than half the population of the Earth—are at risk for hookworm alone, with 807 million currently infected.

What characterizes these particular diseases isn't that—unlike more sensational diseases like HIV/AIDS, malaria and TB—they kill huge numbers of people (about 530,000 people per year, although that is still not nothing). Instead, they are responsible for massive levels of disfigurement and disability, impairing childhood development and economic productivity. They are found in every tropical country (including Australia) and yet are neglected at the community, national and international levels, largely because they affect the poor, the powerless and the stigmatized.

For example, Chagas' disease kills 50,000 people a year (far more than West Nile virus, Bird Flu and Swine Flu combined), but you probably haven't heard of it because it's a disease of the poor. If your house is made of sticks, the bugs that carry the disease burrow through your walls and bite you under the eye. But if you can afford plaster, then you are completely safe. So it is a widespread disease in poor, rural South America (where the average life of a dog is about two years, thanks to the disease), but it doesn't kill anyone who might be in a position to lobby governments, advocate for medical interventions, or mobilize advertising campaigns.

Rather than simply count deaths, the World Health Organization has developed a measure of the number of years of life lost from premature death or disability, or DALYs (Disability-Adjusted Life Years). The number of DALYs per year for HIV/AIDS is 84.5 million. That is, without HIV/AIDS we'd have about 84,500,000 years of healthy life back. But NTDs are collectively the next largest burden on the world, with DALYs of 56.6 million (diarrhoeal diseases are third, followed by childhood and vaccine preventable diseases, then malaria and TB). So despite being neglected, the NTDs are one of the largest problems human beings face today.

Treatments exist for some NTDs, although often control occurs through less “sexy" methods, such as mass dewormings in schools, insecticides, safe water, and, in some cases, arsenic and amputation. (Seriously, arsenic is still used to treat sleeping sickness, while the only treatment for the Buruli ulcer is to amputate infected limbs. NTDs ain't pretty.) Part of the problem is that there is no money in them: why would a profit-driven pharmaceutical company waste time developing treatments for diseases whose sufferers can't pay? Of the 1600 drugs developed between 1974 and 2004, only 18 were for tropical diseases (and three for TB).

So what is to be done? Fortunately, there are a couple of success stories. Guinea worm disease has been all but eliminated, despite having no vaccine, no drug, and no

immunity. Instead, behavior changes (convincing people not to put infected limbs in the water, distributing cloth filters to villages, and outfitting nomadic people with drinking pipes) have led to a massive reduction in cases and already eliminated the disease from Asia and the Middle East.

Who made this miraculous feat happen? It's thanks to the efforts of one man: former president Jimmy Carter, who did the unglamorous but important work of mobilizing public-private partnerships, delivering education messages to remote populations, and even negotiating a "Guinea worm ceasefire" in the Sudan civil war so that NGOs could go in and educate those most at risk. As a result, Guinea worm disease has been almost eradicated from the planet. It is not only going to be the first parasitic disease to be eradicated, it is also going to be the first to be eliminated using behavior changes alone. That's an incredible achievement.

Another success story is river blindness, and this is where mathematical modeling comes into the picture. The West African river blindness program was developed as a co-production between the World Health Organization, the World Bank, the UN, and 20 donor countries and agencies in 1974. Mathematical modeling was used at the outset to predict long-term outcomes; by including modeling in the design of the program, skeptical donors were convinced that control was feasible. When the drug ivermectin was made available in the late eighties, mathematical models were able to adapt to its inclusion. After the program was completed, modeling retained a prominent role in subsequent policy discussions.

One of the great advantages of mathematical modeling is that it's cheap. A lot can be done with a little, so many potential scenarios can be investigated even when data is limited. In a way, this makes NTDs an ideal subject for modeling to tackle. There are a great many problems that urgently need to be solved that mathematical models could help with.

Unfortunately, the NTDs are as neglected by modeling as they are by everyone else. Only sleeping sickness has received any substantial theoretical modeling. There are no models at all for the Buruli ulcer and only one for Guinea worm disease. When models do exist for NTDs, they are usually confined to one lab and its collaborators per NTD. What we urgently need is a diversity of voices.

Specific problems might include adapting malaria pesticide models for vector control in Chagas' disease or leishmaniasis. Spatial modeling is critical: access to resources depends critically upon geographical constraints, so models that account for distance to hospitals, swamps, mountains and road networks are crucial. Co-infection models—between other NTDs and also major diseases like HIV—are also desperately needed.

Modeling could also help categorize the costs to developing economies of disabling NTDs: if treating NTDs is shown to save more money than it costs in productivity, this will help motivate action. Another, slightly meta, approach might be to model research funding itself: if granting agencies are requiring researchers to provide "at home" benefits, this could be standing in the way of significant work on diseases that might help a very large number of people.

In summary, NTDs require immediate attention. They extract an enormous price in suffering, lack of economic development, and the promotion of poverty. Mathematical models can be used to inform policy at minimal cost, solving problems that may not be theoretically complex but have the potential to deliver enormous benefits.

NTDs are the low-hanging fruit of mathematical modeling. A great many problems could be solved, relatively easily, by harnessing the power of mathematical modeling. The price—political and otherwise—for such a huge improvement in the quality of life for one sixth of the world's population is tiny.

Contributor: Robert Smith?
Posted: May 18, 2013

13.6 ▪ Contagious Behavior

There has been some press coverage of an article that appeared in the October 4, 2013, issue of *Science* entitled "Social Factors in Epidemiology" by Chris Bauch and Alison Galvani. The article highlights how social factors and social responses are intertwined in biological systems. For example, a perception that vaccines are harmful can cause a drop in vaccination coverage. The point that the authors make is that mathematical modelers are now creating models that are tailored to include social behaviors into their systems to better predict things like the spread of a disease. Hence, getting clues from social media sources like Facebook and Twitter is useful. (To read the article you need access to *Science*, but a note about the article is available in *Science Daily*.)

While it seems nice to again (as the MPE2013 initiative likes to do) point out the usefulness of mathematics I was struck by how little mathematics was actually in the article. The authors did make a strong case that social factors are important in an anecdotal sort of way, and it did appear that the mathematical models were network-type models, but there seemed to be little of any mathematical substance.

Reading the article I was reminded of the work done by Martina Morris using random network models and the success of those models in predicting HIV spread. Two earlier blogs, from June 6th [3] and the July 2nd [4], showcase the exciting work done by her and other mathematicians using random graph models. There have been several other blogs on this site devoted to modeling disease spread. I found all of these more interesting than the *Science* article. I also wondered how beneficial the work of Morris and others would be for the epidemiology questions asked by Bauch and Galvani. I would speculate quite a bit. I am curious how aware the different researchers are about these and other developments and ironically, if somehow, social behavior of a different sort is at play here.

References:

[1] Chris T. Bauch and Alison P. Galvani, *Social Factors in Epidemiology*, Science **342** (2013) 47–49, DOI: 10.1126/science.1244492.

[2] University of Waterloo. *Facebook and Twitter may yield clues to preventing the spread of disease*, ScienceDaily, 3 October 2013. http://www.sciencedaily.com/releases/2013/10/131003142628.h

[3] http://mpe.dimacs.rutgers.edu/2013/06/06/random-networks-and-the-spread-of-hiv/; cf. Section 13.2.

[4] http://mpe.dimacs.rutgers.edu/2013/07/02/talking-across-fields/; cf. Section 13.3.

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