Spatial deterministic epidemics, by Linda Rass and John Radcliffe, Mathematical Surveys and Monographs, vol. 102, Amer. Math. Soc., Providence, RI, 2003, x+261 pp., $69.00, ISBN 0-8218-0499-5

Bioterrorism: Mathematical modeling applications in homeland security, H. T. Banks and Carlos Castillo-Chavez (Editors), SIAM, Philadelphia, PA, 2003, x+240 pp., $78.00, ISBN 0-89871-549-0

1. Epidemics galore

Some fifty years ago, the World Health Organization expected that the frightening aspects of infectious diseases would soon belong to history and that the threats of the future would lie in non-infectious diseases like cancer and cardiovascular affections. Now, while newcomers like HIV-AIDS and SARS make the headlines, old-timers like malaria and TB again make victims by the millions. On top of that our livestock is hit by BSE, foot-and-mouth disease, classical swine fever and avian flu, causing gigantic economic losses despite draconic control measures which are highly debatable from an ethical point of view. Plant improvement is pretty much an arms race against co-evolving pests. Finally, the prospect of bacteria developing resistance against ALL available antibiotics is terrifying indeed.

No doubt, therefore, that infectious agents and their propagation deserve our attention. For future oriented speculations see Ewald (1994) and Garrett (1994), but don't underestimate the role they played in the past in shaping the world as we know it now; see Diamond (1997), McNeill (1979), Winslow (1980).

2. About outbreaks and control

Infectious agents may cause epidemic outbreaks or circulate continuously (with a prevalence that may be roughly constant or may show considerable fluctuations, with a periodic or even chaotic pattern). There are multiple reasons why the outbreak situation is of special interest. First, from the perspective of the agent, the "virgin" host population constitutes the ideal world, as the amount of "fuel" is not yet diminished by provoked immunity. Or, in other words, an agent that cannot make it in a virgin host population can, as a rule, not make it at all. (There are exceptions, van den Driessche and Watmough (2002), but their relevance for actual host-microparasite systems is yet to be demonstrated; for macroparasites (worms) that mate inside a (primary) host the phenomenon of positive density dependence (meaning that individuals benefit from higher population density) is certainly relevant; see Nåsell (1985).) The second reason derives from this rule: if we want to drive an endemic agent to extinction, we should create conditions in which it would have failed to establish itself. So the potential impact of control measures can be ascertained in thought experiments in which we pretend that the agent enters a virgin host population, even though in reality the agent has a firm foothold. A third reason is that the agent may very well create a large outbreak, yet

fail to become endemic. This may be due to immunity, when there exists a major timescale difference between the rise and fall of the epidemic on the one hand and the demographic turnover of hosts on the other hand (the classic example is measles on Iceland; Cliff, Haggett and Smallman-Raynor (1993)). But it may also be due to control measures, such as in the case of foot-and-mouth disease in Britain in 2001; see Keeling et al. (2003) and Ferguson, Donnelly and Anderson (2001). In such situations we have to deal with possibly repeated outbreaks rather than endemic prevalence levels.

3. TRANSIENTS COUNT

An agent that provokes immunity in a host that has a life span which is rather long compared to the time scale of transmission from one host to the next may trigger an epidemic outbreak that burns like a fire in which flames and heat reach enormous heights; yet, like the fire, it is bound to go extinct eventually due to lack of fuel. So the dynamics is rather simple if we ignore demography all together: a steady state, called 0 and corresponding to the virgin host population, is unstable, and any biologically realizable perturbation (an introduction of the agent), no matter how small, gives rise to a sequence of events (an orbit) which ends in another steady state, which we call x_∞. Despite the dynamical simplicity one can ask a difficult question: how long will the transition from 0 to x_∞ effectively take? The sting is in the adverb "effectively", which makes the mathematically correct answer "it takes an infinite amount of time" inappropriate. The mathematical theory of dynamical systems centers around the asymptotic, for large time, behaviour of trajectories and, in particular, the classification of structure and stability of invariant sets. Transients are the Cinderellas which do the work but which are hardly ever regarded as interesting by themselves.

The initial phase of the transition is governed by the linearization near 0, the intermediate phase by the nonlinearity of the contact process underlying transmission, and the final phase by the linearization near x_∞. Each has its characteristic timescale. But a farmer finding his cornfield invaded by a rust wants to know how much of the field is affected at harvest time in order to decide whether the costs of spraying are (far) less than the economic loss when nothing is done. This limits the time window of interest but adds a spatial dimension to the problem. At first sight, this only seems to complicate the matter but, as we will see, it actually enables us to bring asymptotics back into play.

4. SPREADING LIKE WILDFIRE

Do infectious diseases spread spatially like wildfire? Some do. For instance, many fungal infections expand with an almost constant speed in agricultural crops if not opposed by pesticide application. And the Black Death in medieval Europe spread similarly, though of course influenced by the inhomogeneities of mountains, lakes, etc. (see Noble (1974) and for more general "pictures" Cliff and Haggett (1988)). So assume, as an idealization, that the field extends infinitely far in all directions and is both homogeneous and isotropic. Then we can rephrase the question and ask: how fast does the region in which the local state is near x_∞ grow?

In 1975 D.G. Aronson and H.F. Weinberger introduced, in the context of nonlinear diffusion equations, the notion of the "asymptotic speed of propagation" of disturbances. The idea is to inflate a ball such that its radius increases with speed

c and to restrict attention to either the inside or the outside. If c_0 is such that, asymptotically for large time,

> the local states in the inside are near x_∞ if $c < c_0$ and
> the local states in the outside are near 0 if $c > c_0$, provided we limit the introduction to a compact set,

we call c_0 the asymptotic speed of propagation (of disturbances). The notion is both easily formulated precisely in mathematical terms and excellently adapted to the biological substratum. So clearly we should answer our question with "the speed equals c_0" if such an asymptotic speed of propagation exists. But does it exist? And if so, how can we characterise c_0 in a way that allows us to compute it (numerically, if necessary)?

The (assumed!) homogeneity implies that the problem is invariant under translation. A self-similar solution is a solution such that the progress of time is captured by a translation in space (see Barenblatt (2003) for the general idea). Or, in other words, a self-similar solution is a travelling plane wave

$$u(t,x) = w(x.\nu - ct)$$

with profile w, speed c and direction ν. The (assumed!) isotropy implies that the direction ν is irrelevant: if such a solution exists for a particular ν, it exists for any ν. So the problem amounts to finding a function w of one variable (the profile) and a real number c (the speed). This is substantially easier than finding arbitrary solutions that are functions of the TWO variables t and x. Our interest in these special solutions derives from the idea that an observer moving with the right speed might be able to study the transients. Or, in other words, in a moving coordinate system the transients may look like a "frozen" spatial transition.

The book by Rass and Radcliffe centers around a robust fact (highlighted already by Aronson and Weinberger): travelling plane wave solutions exist for all speeds c exceeding some c_0, and the minimal wave speed c_0 IS the asymptotic speed of propagation of disturbances. The following argument (due to J.A.J. Metz) makes the result intuitively understandable. By manipulating the initial condition suitably, we can produce travelling waves in much the same way as one can create the illusion of steady movement in an array of electric lights by turning them on (and off) appropriately. In other words, a pre-arranged ignition pattern shows up as a travelling wave. Only one thing can spoil this game: if we try to make the speed too low, the inherent "infection" mechanism of our excitable medium takes over. In other words, if a spot ignites its neighbour, we can't pre-arrange the ignition. Therefore this inherent infection speed is exactly the lowest possible wave speed!

The convergence of solutions of the Initial Value Problem towards travelling wave solutions is a subtle matter when there is a continuum of wave speeds; see Bramson (1983) and van Saarloos (2003). The notion of "asymptotic speed of propagation" avoids the technical complications of convergence of profiles while providing the relevant biological information!

It is an experimental fact, derived from simulation studies, that the quantity c_0 is highly relevant for a description of propagation in FINITE (but large) fields during FINITE time intervals. In his book from 1979 G.I. Barenblatt writes:

"Self-similar solutions also describe the 'intermediate asymptotic' behaviour of solutions of wider classes of problems in the range where these solutions no longer

depend on the details of the initial and/or boundary conditions, yet the system is still far from being in a limiting state."

If we think again about a fungal pest of an agricultural crop, we are describing the expansion of a focus in one field. Occasionally spores may rise high above the canopy and travel, blown by the wind, over large distances. So if we are interested in spread on a larger geographical scale, we need to incorporate rare but very influential events, such as what happened in the case of SARS, where, on top of the common local transmission, air travel provided incidental large distance transmission. In other words, the regular wavelike expansion doesn't always tell the full story. A related point is that we should worry about demographic stochasticity. Deterministic statements concerning a small FRACTION of a large host population ignore the initial phase in which a small NUMBER may or may not grow to a small fraction. This initial phase should be described by a branching process which, even when supercritical, may go extinct; see Haccou, Jagers and Vatutin (2005).

5. The pioneers

The work of Aronson and Weinberger had its roots in the work by Fisher (1937) and Kolmogorov, Petrovsky and Piscounov (1937), and that of Skellam (1951, 1973). Fisher and KPP were interested in the speed with which an advantageous allele (created at some position by mutation) would spread. Skellam wanted, among other things, to understand the population wave of invasion into "empty" territory (like oaks after the Ice Age or species introduced by humans into foreign continents in which they didn't occur before; see Hengeveld (1989) and Shigesada and Kawasaki (1997)). In the epidemic context, Kendall (1965) was the pioneer, later followed by his student Mollison (1977); rumour has it that Kendall obtained his results during the Second World War but that he postponed publication, fearing that they might trigger exactly the kind of situation that motivates the contributions to the book edited by Banks and Castillo-Chavez.

6. The methods

For diffusion equations, one can use phase plane analysis to find travelling plane waves as heteroclinic orbits; see Aronson and Weinberger (1978). The information obtained from the phase plane analysis can also be used to construct lower solutions that allow us to derive strong conclusions through a comparison method based on the maximum principle.

Rass and Radcliffe deal with host-vector models (the "vector" is the carrier, or secondary host (for instance a mosquito), that brings the parasite from one primary host to the next) and spatial redistribution described by integral operators (cf. Weinberger (1982)). Still the comparison method is the key tool, but many aspects require a new approach. Figuring out what tools are needed (or, at least, do the job) is as always the key to success. Would you guess that Ikehara's Tauberian Theorem, Feller's Renewal Theorem and a rather abstract convolution inequality are featured in various proofs?

7. The context

For an excellent introduction to the varied mathematical approaches (and their equally varied ecological motivations) in spatial ecology in general, see Dieckmann, Law and Metz, eds. (2000). The books Cantrell and Cosner (2003) and Okubo and

Levin (2001) focus on diffusion models, and Tilman and Kareiva (1997) is intended for the less-mathematically minded ecologist.

Concerning the epidemiology of infectious diseases, Anderson and May (1991), Becker (1989), Diekmann and Heesterbeek (2000), Hethcote (2000) and Part 3 of Thieme (2003) can be consulted for introductory surveys of various aspects and a wealth of references (also see Section 8.2 of Newman (2003)).

Understanding the evolutionary battleground between parasite and host is quite a challenge (our intuition isn't trained to look at short-term selfishness from a long-term perspective). The carefully edited collection of papers Dieckmann et al. (2002) provides an overview.

8. Comparing the two books

The qualitative understanding of the spatio-temporal pattern arising in the context of idealized models is one thing; deciding about control actions on the basis of rather limited (perhaps even inconsistent) data is quite another thing. Without any doubt (and as testified by the Rass-Radcliffe book), mathematics is rather efficient in providing the first. The book edited by Banks and Castillo-Chavez explores hesitantly the usefulness of mathematics to aid the second, in particular when an infective agent would be introduced deliberately in what is called the "homeland".

The two books form the two extremes of a spectrum. Where Rass and Radcliffe are concerned with a well-established understanding based on rigorous and highly nontrivial mathematical analysis of one particular aspect of the epidemiology of infectious diseases, Banks and Castillo-Chavez address the challenge of preparing for the unknown by way of models and methods yet to be developed.

In Rass-Radcliffe we see the pure form of applied math at its best: a meaningful biological problem is reduced to its mathematical essence, the right concepts (in particular the notion of "asymptotic speed of propagation") are introduced, ingenious techniques to analyse the problem are developed, the key result (here "minimal wave speed = asymptotic speed of propagation") is first proved in the simplest situation and subsequently generalized to more complicated situations (like host-vector).

The "dirty but useful" form of applied math aims to draw conclusions from data and helps to choose, when confronted with a problem in real life (as opposed to "in mathematics" where "problems" are often "nice" or even "beautiful"), from various possible actions on the basis of a convincing rationale. It requires a different form of ingenuity and exerts a different form of appeal.

Will the twain meet in the long run? In any case, they should be confronted. For it is at the interfaces where usually the most interesting progress is made.

Does the monitoring by the Centers for Disease Control lead to an alert when needed, and do we have models to guide our actions? It is clear that surveillance, modelling and data analysis require knowledge, tools and ingenuity and that the timescale at which action may be needed can be so short that any preparation pays off. But the word that occurs most frequently in the bioterrorism book is "potential", so let's hope that we shall never have to find out whether or not this book has anything to offer and that the science fiction of Margaret Atwood (see `http://www.oryxandcrake.co.uk/`) remains something one should not discuss in the *Bulletin of the AMS*.

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