

Mathematical models of the spread of infection

DAVID G. KENDALL

There have been several interventions by mathematicians and statisticians into the field of epidemiological theory. At the moment, however, it is difficult to justify the mathematical models by reference to specific diseases because the main task is to learn what qualitative behaviour to expect of the very simplest models of contagion which might be postulated. Almost certainly these models are ridiculously over-simplified. Often they could be made more realistic by introducing a much larger number of additional mechanisms, each with its own array of arbitrary constants; in most cases the analysis of such variations does not introduce any new difficulties of principle, and does not necessarily lead to any better understanding of the basic problems. The deterministic threshold phenomenon was discovered by Kermack and McKendrick in connection with epidemics in isolated compact communities, and recent work by a number of statisticians has shown that the deterministic differential equations can be replaced by a stochastic model which makes allowance for the role of chance in determining the course of an outbreak. Further inquiries about the qualitative behaviour of such models may demand use of rather more sophisticated mathematical techniques, and this can be seen in recent work on the speed of propagation of contagious phenomena (the simplest possible example being in the linear community).

1. This survey is selective, and the topics selected will be those on which I happen to have worked myself. The inspiration for them all is the 1927 paper by Kermack and McKendrick, and it is worth noting that these two pioneers of a new branch of applied mathematics were not themselves professional mathematicians. Kermack is Professor of Biological Chemistry in Aberdeen, and McKendrick was a lieutenant-colonel in the Indian Medical Service (later working in the Laboratory of the Royal College of Physicians in Edinburgh). Mathematicians may be blamed for subsequently carrying the game too far, but its highly respectable medical origin should not be overlooked.

There is a tendency to distrust mathematicians when they write on medical topics, so perhaps I had better begin by saying what I believe to be the value of and justification for work of the kind reported here. In general I have little confidence in any but the *qualitative* predictions; I expect the usable results to be not numbers but a list of possible modes of behaviour. Also I consider the ultimate justification for this sort of work to be the fact that precisely similar grossly over-simplified models are talked about (in words, if not in symbols), or perhaps only thought about, by all who are professionally concerned with epidemics, their natural history, and their prevention. There have always been theories about epidemics, as readers of Manzoni's *I Promessi Sposi* will recall, and if we are to have theories then we might as well be precise about what their consequences would be if the theories were true. To know the consequences may be to reject the theory, but this is one way in which truth prevails.

2. In the paper just mentioned Kermack and McKendrick were concerned with a 'model' of epidemics which was special in at least three respects, and which was deliberately made as simple as possible (not because Nature is simple, but because they were trying to build up an understanding of how such systems function, and one must understand the simplest versions first). The three respects in which their model was special are these: (i) the population concerned was supposed to be isolated from the rest of the world (McKendrick mentioned a ship taking immigrants to Australia, and nowadays one might prefer to think of a space-ship); (ii) the initial degree of contact between members of the population was supposed to be the same for each pair (a democratic regime); finally (iii) the model was a deterministic one rather like those used in the discussion of mass-action phenomena in physical chemistry, and the individual and chance character of infection was at this stage glossed over.

Specifically one divides the (finite, constant) population into three groups: susceptible individuals, x in number; infectious individuals, y in number; removed cases, z in number; thus $x+y+z$ is fixed and equals the population size. Here it must be emphasized that 'removed cases' includes infectious persons who have been isolated and so are no longer active in spreading infection, as well as those who are dead, and those who have recovered and are now immune. (Recovery without immunity can easily be incorporated into the model, as can also the possibility of subclinical infection, and of 'carriers'; these possibilities are excluded here so that attention may be focussed on the pure phenomenon of contagion itself.) As Professor M. S. Bartlett has remarked in a rather grim aside, the z -state is that from which there is no return.

We now suppose that only the following elementary transitions are possible:

- 'infections': $x \rightarrow x-1$ and $y \rightarrow y+1$;
- and
- 'removals': $y \rightarrow y-1$ and $z \rightarrow z+1$.

(Subclinical infections conferring immunity and not contributing further to the spread of the epidemic would correspond to transitions like $x \rightarrow x-1$, $z \rightarrow z+1$, and so on). A product-law is assumed for the rate of occurrence of infections, giving the differential equation

$$dx/dt = -xy \tag{1}$$

(where the unit of time is chosen so that no constant multiplier is required), and removals are supposed to take place at a rate proportional to the size of the group from which they occur, so that (1) is coupled with the sister-equation

$$dy/dt = +xy - \rho y, \tag{2}$$

where ρ is a positive dimensionless constant which we cannot dismiss because we have already made full use of the freedom to choose our time-units. This constant ρ can be thought of as the ratio between the removal rate when $y=n^2$ and the infection rate when $x=y=n$.

From (1) and (2) we at once find that the value of the expression

$$\phi(x, y) = x + y + \rho \log(\rho/x) \tag{3}$$

(natural logarithms) does not change with time, so that we have a 'law of conservation of ϕ -ness'.

Now suppose that we start at $t=0$ with n susceptibles and with a very small number ϵ of infectious persons (small with regard to ρ). Then we can draw up a sort of balance-sheet (before and after the epidemic) as follows:

<i>before</i>	
$x = n$	<i>after</i>
$y = \epsilon$	$n - E$
$\phi = n + \epsilon + \rho \log(\rho/n)$	$n - E + \rho \log \left(\frac{\rho}{n - E} \right)$

Here E is the number of the n initial susceptibles who 'catch it'; we may call E the size of the epidemic.

If we equate the two values of ϕ we discover that

$$1 - \frac{E}{n} = C e^{-E/\rho}, \tag{4}$$

where $C = e^{-\epsilon/\rho}$ is less than (but only just less than) unity. Drawing a graph of $v = 1 - E/n$ and $v = e^{-E/\rho}$ then shows at once that E is very slightly greater than the largest root of the equation

$$1 - \frac{E}{n} = e^{-E/\rho}, \tag{5}$$

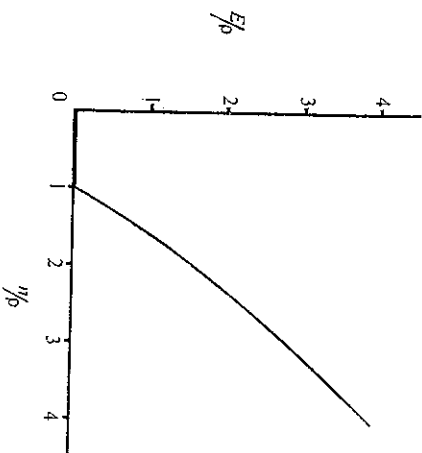


Figure 1

The relation between the size, E , of the epidemic and the number, n , of susceptibles, when the threshold is ρ (E/ρ is plotted here against n/ρ).

and that E approaches this root as $\epsilon/\rho \rightarrow 0$. Figure 1 shows a graph of the relevant root E , plotted against n (actually we plot E/ρ against n/ρ). It will be seen that there is a sharp break in behaviour at the critical value $n = \rho$:

- when $n \leq \rho$, then a trace of initial infection will produce virtually no epidemic;
- when $n > \rho$, a trace of initial infection, HOWEVER SLIGHT, will produce an epidemic of size AT LEAST equal to $E > 0$.

This is the core of the famous Threshold Theorem of Kermack and McKendrick, which elucidates 'why', in respect of a given disease and given circumstances of contact and so on, there is a critical population size (equal to the threshold, ρ) below or at which school classes, lecture audiences etc. should be kept, if major outbreaks are to be avoided.

All this and much more is in their 1927 paper; for example they determine the temporal history of an outbreak, and they develop approximations for the root of the equation (5) when n is only just greater than ρ (e.g., $E \approx 2(n-\rho)$). The importance of these approximations has perhaps been too much stressed, and in my view it is the *existence* of a threshold, and not the predicted size of the outbreak, which is the important outcome of the investigation. This is an example of what I had in mind when I spoke of attaching importance only to the qualitative predictions.

3. Those who are interested in the actual sizes of thresholds can refer to the excellent book by Bailey (1957). Of course the threshold effect is a consequence of the particular sorts of contagion and 'removal' which we have described; it would be incorrect to deduce that there must be a threshold for all maladies, however generated or conveyed. Thus one might (and I once did) suppose that the mechanism for the dissemination of a rumour would be very similar to that for an epidemic, but a current investigation by Daley and myself (1965) shows this not to be so; with a model for rumour transmission which we find quite natural there is *no* threshold.

In view of this we ought to recall the over-simplified character of our epidemic model and suspect that perhaps the threshold effect would disappear or at least be profoundly modified if assumptions (i), (ii) and (iii) were varied. The effect of varying (i) by allowing the regular introduction of new susceptibles (e.g. children of school age) leads to the Hamer-Soper-Bartlett oscillatory models for measles (Bartlett, 1960: chapter vii), which there is no room to describe here. I shall say something in §4 about the effect of relaxing (ii), and wish now to look at the effect of relaxing (iii) by taking proper account of the fact that x and y are capable only of integer values, and change only by jumps, and by random jumps at that.

The need for such a discussion was fully appreciated by McKendrick, and his paper of 1926, in which he formulated and partly solved the problem, must be accounted one of the classical texts of the theory of stochastic processes. He there uncovered only half the story, and it was not until some thirty years had passed that a combination of the work of Bailey (1953), Bartlett (1955), Whittle (1952, 1955) and myself (1956) showed both what happens and 'why'. To remind us that the numbers of susceptibles and infectious persons are now whole numbers, we shall write X and Y in place of x and y , and we shall take $X=N$, $Y=1$ at the initial instant $t=0$. In time (t , $t+dt$) we give the transition

$$X \rightarrow X - 1, \quad Y \rightarrow Y + 1 \quad (\text{an infection})$$

the probability $XYdt$, and we give the transition

$$Y \rightarrow Y - 1, \quad Z \rightarrow Z + 1 \quad (\text{a 'removal'}),$$

the probability ρYdt , all other possibilities (save that of 'no change') in this elementary time-interval having probability $o(dt)$, and we make the usual assumptions of Markov character to exclude the complicating effects of 'memory' or 'hysteresis' in the system. We then find that the situation, as before,

is on the whole quite different in the two cases $N \gg \rho$ and $N \ll \rho$, so that we may still very properly speak of ρ as the threshold, but what now happens in the super-critical case (number N of susceptibles above the threshold) presents new features which may at first be found surprising.

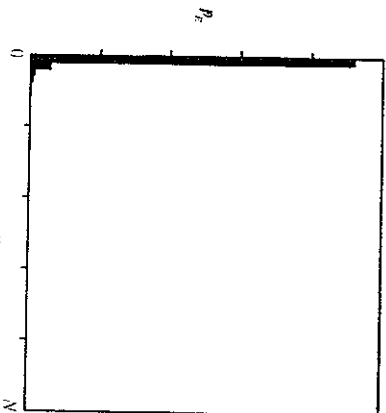


Figure 2
The distribution of the size, E , of a stochastic epidemic when $N = \rho/2$ ($N = X(0) = 200$, $Y(0) = 1$) (the value of E ranges from 0 to N along the horizontal axis).

In the sub-critical case (when $N \ll \rho$) we have, not *no* epidemic, as previously, but a minor outbreak of random size. This is illustrated in Figure 2, where the horizontal axis shows the range (from 0 to N) through which the size E of the epidemic can conceivably vary, and the vertical axis shows the frequency with which epidemics of each possible size will be generated in the given conditions, which are $\rho = 400$, $N = X(0) = 200$, $Y(0) = 1$ (so that $N = \rho/2$). The area of the heavily shaded region is equal to unity (unity of total probability), and it will be seen how heavily the very small values of E are weighted in this case. (The calculations on which this diagram and the next are based were the results of one of my first Mercury programs written after a three-day course at Professor Fox's Laboratory in Oxford. I mention this both in gratitude to him and his staff, and also to show how quickly even a mathematician, notoriously the type of person least likely to succeed at arithmetic, can learn at least the elements of automatic computing.)

In the super-critical case (when $N \gg \rho$) the state of affairs is startlingly different. It is illustrated by Figure 3, where we show exactly as in Figure 2 what happens when $\rho = 100$, $N = X(0) = 200$, and $Y(0) = 1$, so that now $N = 2\rho$. This time it will be seen that we have a probability-distribution consisting of two virtually distinct lumps, one still located near $E=0$ but the other centred near $E=160$, which would have been the value of E predicted by the earlier (deterministic) model. What happens in a super-critical situation is that we are then dealing with a system capable of two quite different modes of behaviour; on any given occasion one or other of them will be realized but in *principle* one cannot foretell which. Either there will be a minor outbreak (much as if we were after all in the sub-critical case) or there will be a major outbreak of roughly the size the older (deterministic) theory would have predicted.

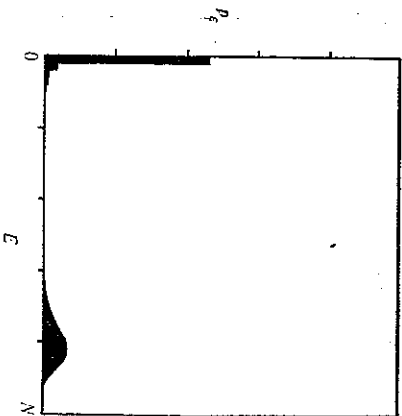


Figure 3
The distribution of the size, E , of a stochastic epidemic when $N=2\rho$ ($N=200$, $Y(0)=1$) (the value of E ranges from 0 to N along the horizontal axis).

Now all this is in fact entirely reasonable. In the first place it is plain that there is always at least an outside chance that the one initial infectious person will be 'removed' before he has had the chance to infect any one else, or, more generally, that by chance and (our) good luck the epidemic will peter out quickly even though conditions are generally favourable (to it) for rapid extension. Thus, even when $N \gg \rho$, we must not be astonished to see some probability lingering near $E=0$. If, however, the epidemic does manage to get under way, one might expect the older theory to work reasonably well as soon as the numbers concerned have built up to large values, and thus we are not after all astonished that the epidemic size, if it is large, will usually turn out to have about the deterministic value.

This raises an interesting question. If we are in the super-critical situation, with what probabilities will the two sorts of behaviour occur: i.e. if $N \gg \rho$, how frequently will we be lucky, and how frequently will the epidemic be lucky? This is, of course, to ask what are the amounts of probability located in the two lumps into which the distribution has now broken. The approximate answer (when everything stems from a single initiating case ($Y(0)=1$)) is:

$$P(\text{minor outbreak}) = \rho/N, \quad P(\text{major outbreak}) = 1 - \frac{\rho}{N}. \quad (6)$$

More generally, when $Y(0)$ may be greater than unity, (6) is replaced by

$$P(\text{minor outbreak}) = (\rho/N) Y(0), \quad P(\text{major outbreak}) = 1 - \left(\frac{\rho}{N}\right) Y(0). \quad (7)$$

The transition from (6) to (7), at least, is easy to comprehend, for to a first approximation, for early values of t , we may treat as independent the cases resulting from each of the $Y(0)$ initial cases. Thus, if a single 'clone' of cases has a chance ρ/N of petering out, the chance for $Y(0)$ independent such 'clones' will be roughly the $Y(0)$ th power of the former probability.

One can also explain the whole of (6) in much the same way. Let us fix attention on the $Y(t)$ infectious persons only, and think of the history of this sub-population as a problem in the theory of stochastic population growth, which reached a fairly advanced stage of development in the late nineteenth forties and is now sufficiently old-fashioned to feature in many mathematical examination syllabuses. We must now think of an infection as the *birth* of a Y -man, and of a 'removal' as (what it may well be in fact) the *death* of a Y -man. Then we have a stochastic birth-and-death process (for which see e.g. Bartlett, 1955; Kendall, 1949, 1952), with a birth-rate $X(t)$ (nearly equal to N , when t is small), and a death-rate ρ . Continuing to think only about the period in which t is small and the chance effects are still dominant, we see that when $N < \rho$ we shall have a sub-critical birth-and-death process, doomed to almost certain extinction, and that when $N > \rho$ we shall have a super-critical birth-and-death process allowing two possibilities:

extinction, with probability ρ/N ,
explosion, with probability $1 - \frac{\rho}{N}$.
and

The 'extinction' option yields a minor outbreak, while with the 'explosion' option the numbers build up rapidly and the deterministic solution takes over.

The results summarized here constitute what is sometimes called the Stochastic Threshold Theorem; a more detailed account of this approach will be found in Kendall (1956). (For a different treatment, see Whittle, 1952.)

To those not previously familiar with birth-and-death and branching processes it may be remarked that a terrible example of this theory is to be found in Hiroshima. It can be traced to a rather Danish inquiry in 1873 by Sir Francis Galton (1889) on the statistics of surnames*, and it reappeared independently in 1922 in an investigation by Sir Ronald Fisher into the extinction of rare genes. A further example arises in what is sometimes called queuing theory (Kendall, 1951). Ideas with such wide relevance and appalling effect command our attention.

4. I promised to say something about the effect of relaxing (ii), the assumption of 'uniform propinquity'. Of course it is never satisfied; especially when N is large we must take account of the facts that the individuals in the population will be geographically (and perhaps also sociologically) dispersed, and that infection will be more likely between close neighbours than between well separated pairs. One can begin to formulate this problem in many ways, and I will confine myself here to the sector of the theory which is most fully worked out; it has not been published before, and will not be published in full mathematical detail here. We shall confine our attention, then, to a one-dimensional population, uniform in density, and we shall look into the possibility of waves of infection travelling along this linear community. Two-dimensional versions could be worked out similarly, but would be more complicated in detail. It is believed that the analysis developed here has some relevance to what happens at the spreading edge of a pandemic (like the world-wide epidemic of 'Asian' influenza). Naturally in practice immense further complications are present—several types of virus, innate immunity, re-infection, and so on. I hope, however, after what has been said about the closed epidemic models, that I will not now be accused of *flagrantly* unrealistic over-simplification.

*See also Kendall (1949) for earlier references.

I shall describe the deterministic theory only, for the good reason that no other exists as yet. Suppose then that σ is the density of individuals living on our line (in persons per mile, say) and that at time t and position s along the line the local density of susceptibles is $x(s,t)\sigma$, and of infectious persons, $y(s,t)\sigma$. The analogue of equations (1) and (2) will now be

$$\frac{\partial x}{\partial t} = -xy, \quad \frac{\partial y}{\partial t} = +xy - (\rho/\sigma)y. \tag{8}$$

Here we have as before taken advantage of the possibility of absorbing one constant into the scale in which time is measured, and there remains the constant ρ which now has the dimensions of a density (like σ). Partial time-derivatives are used because x and y are now functions of the space-variable s as well as of the time-variable t , and \bar{y} (a local spatial average of y) occurs instead of y in the second-degree infection terms in (8) because we want to take account of the fact that a susceptible at position s can be infected by infectious cases in the neighbourhood of this point. The weighting function implied in the transition from y to \bar{y} will take into consideration the greater risk of infection between closer pairs.

Now equations (8) as they stand are still rather difficult to handle, and we therefore modify them in two different ways. First we approximate to the local average \bar{y} by using instead

$$y + k \frac{\partial^2 y}{\partial s^2}, \tag{9}$$

where $k > 0$. (This is reasonable if \bar{y} is a short-range symmetrical average.) Thus $\bar{y} > y$ if y is locally convex, and $\bar{y} < y$ if y is locally concave. We shall get nonsense results if the second space-derivative of y is less than $-y/k$; fortunately this does not happen. The second modification is that instead of trying to find the most general solution to (8), we look only for travelling waves, by putting

$$x(s,t) = x(s - ct), \quad y(s,t) = y(s - ct), \tag{10}$$

where $c(>0)$ is the velocity with which the wave travels (the form of the wave being preserved).

It is useful to have $S = s - ct$ as a label for the single argument of x and y . When S is large and positive we will be ahead of the wave, and we shall therefore want

$$x = 1, \quad dx/dS = 0, \quad \text{and} \quad y = dy/dS = 0 \quad \text{at} \quad S = +\infty. \tag{11}$$

When S is large and negative we shall be in the wake left behind by the wave and we shall therefore want

$$x < 1, \quad dx/dS = 0, \quad \text{and} \quad y = dy/dS = 0 \quad \text{at} \quad S = -\infty. \tag{12}$$

The variable S can be used to locate phenomena relative to the frame of axes travelling (with velocity c) with the wave, but we can use $x(S)$ instead because we shall have, from (8),

$$cx' = x(y + ky''), \quad cy' = -x(y + ky'') + (\rho/\sigma)y \tag{13}$$

(where $'$ denotes differentiation with respect to S), so that dx/dS is positive. As we travel along and relative to the wave, y will vary, and so it can be expressed as a function of x . It turns out on calculating dx/dS and dy/dS that

the whole problem can be reduced to the solution of a differential equation governing y as a function of x ; this is

$$\frac{dy}{dx} = \frac{U(x) - y}{by - U(x)}, \tag{14}$$

where $b = 1 + (k/\lambda^2 c^2)$, $\lambda = \sigma/\rho$, and

$$U(x) \equiv 1 - x + \lambda^{-1} \log x.$$

We have to look for a solution-curve terminating (for $S = +\infty$) at $x = 1$, $y = 0$, and starting (for $S = -\infty$) at $x = \alpha$ ($0 < \alpha < 1$), $y = 0$. Also the expression (14) for dy/dx must be indeterminate at each extremity, * which means that we must have $U(\alpha) = 0$. Now U cannot have a zero in $(0,1)$ unless $\lambda \geq 1$, i.e. unless $\sigma \geq \rho$; i.e. unless the population-density exceeds a threshold value, ρ . This may be called the Threshold Theorem for Waves. In what follows we suppose the condition satisfied, and we look for a suitable trajectory satisfying (14) and going from the singularity at $(\alpha, 0)$ to that at $(1, 0)$.

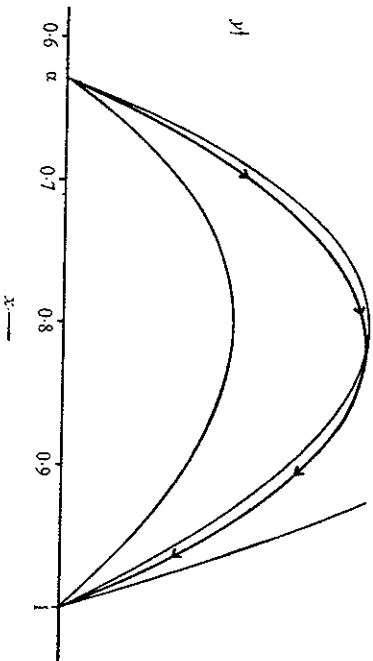


Figure 4

Illustration of the proof that all velocities $c \geq c_{min}$ are possible (here x is abscissa and y is ordinate, and the 'arches' relate to the curves $y = b^{-1}U(x)$, $y = U(x)$, and $y = \beta U(x)$ (incomplete). The curve marked with arrows shows the trajectory emerging from $(\alpha, 0)$ and travelling to $(1, 0)$.

Routine application of the perturbation theory for autonomous systems shows that there is a unique trajectory emerging from $(\alpha, 0)$, and that it lies in the zone between the curves $y = U(x)$ (call this C_1) and $y = b^{-1}U(x)$ (call this C_2). The situation is illustrated in Figure 4. The trajectory cannot cut C_1 (except at a singularity) unless it has a 'horizontal' tangent, and it cannot cut C_2 (except at a singularity) unless it has a 'vertical' tangent. In the 'lens' bounded by C_1 and C_2 it must increase, and above C_1 it must decrease. Thus the trajectory coming out of $(\alpha, 0)$ must cross C_1 on the right-hand side of the 'arch' and then turn downwards. Will it hit $(1, 0)$? The theory shows that it cannot do so when $c < c_{min}$ where

$$c_{min} = 2 \left(k \frac{\sigma - \rho}{\sigma} \right)^{1/2}, \tag{15}$$

* Because $dx/dS = dy/dS = 0$ at $S = \pm \infty$.

because then all solutions near $(1,0)$ must be spirals and must wind again and again into the forbidden half-plane $y < 0$. Thus no waves are possible with a smaller speed than this. What happens when $c = c_{\min}$ or $c > c_{\min}$? It turns out that then the route we have followed out of $(\alpha, 0)$ will always hit $(1,0)$ from above, and therefore that waves are possible with every velocity greater than or equal to c_{\min} .

The proof of this rather surprising fact is of the same elementary differential-topological character as the rest of the argument sketched above; it was suggested by a step in the proof of a theorem of Kolmogorov, Petrovsky and Piskunov (1937), who showed in a rather similar, genetical problem (the wave of advance of an advantageous gene) that all velocities at or above a certain minimum are possible. The trick consists in considering the relation between the trajectory and a further 'arch' C_3 in the (x, y) -plane, with equation $y = \beta U(x)$, where the constant β is chosen so that everywhere on C_3 the gradient dy/dx of the trajectory will be equal to the gradient $\beta U'(1)$ of C_3 at $(1,0)$. Such a value of β can always be found if $\lambda > 1$ and $c \geq c_{\min}$, and we then find that the trajectory which we are following cannot cross the right-hand side of the 'arch' C_3 , and so is forced down into the 'cusp' between C_1 and C_3 , to terminate at $(1,0)$.

The fact of the indeterminacy of velocity in the genetical problem was independently discovered at about the same time by Sir Ronald Fisher (1936); the investigation by the Soviet mathematicians contains the further very significant result that in that problem an initial discontinuity of arbitrary form (but of spatially restricted extent) will generate a wave travelling ultimately with the minimum velocity. It therefore seems likely that in the epidemic problem an initial spatially local concentration of infectious persons will generate two waves (travelling towards $s = -\infty$ and $s = +\infty$) having asymptotically the velocity c_{\min} . We have seen that waves of every velocity greater than this are

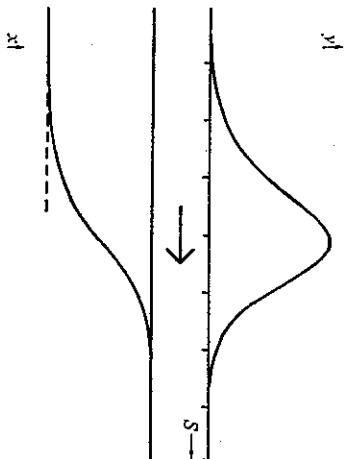


Figure 5

The profile of an epidemic wave when $c = c_{\min}$, $\lambda = 1.25$ (the upper (peaked) curve is the plot of y against S ; the lower one (on a different vertical scale) is the plot of x against S).

possible, but the initial disturbance needed to generate them could not then be of local character. It is also likely that the high-speed waves are unstable, in the sense that under perturbation they will break up into wavelets travelling with the minimum speed, and if this is so then essentially only the minimum speed should be relevant in a stochastic solution. These questions have not yet been fully resolved, and are being further investigated.

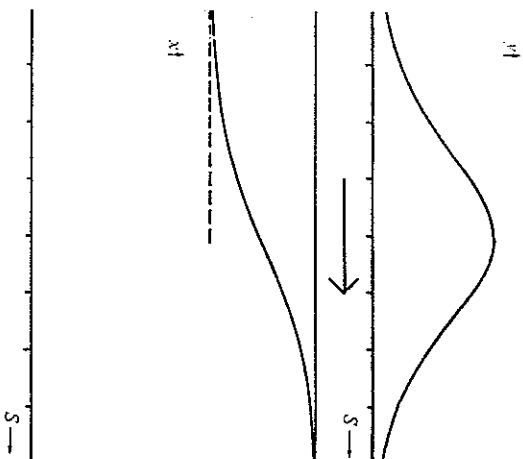


Figure 6

The profile of an epidemic wave when $c = 2c_{\min}$, $\lambda = 1.25$ (the upper (peaked) curve is the plot of y against S ; the lower one (on a different vertical scale) is the plot of x against S).

Figures 5 and 6 show the cross-sections of the waves (i) with the minimum speed and (ii) with twice the minimum speed, when the population density σ is twenty-five per cent above the threshold, ρ . It will be noticed that the faster wave is about twice as 'thick' as the minimal one, when measured in spatial terms, so that the profiles of the two waves would be about the same when measured (in time) by a stationary observer.

I should like to conclude by thanking Dr M. V. Wilkes and the staff of the University of Cambridge Mathematical Laboratory for assistance with some of the wave calculations (which were performed on EDSAC II). I also want to thank Professor M. S. Bartlett and Professor G. E. H. Reuter for numerous discussions of these problems.

- Bailey, N. T. J. (1953) The total size of a general stochastic epidemic. *Biometrika* 40, 177.
 Bailey, N. T. J. (1957) *The mathematical theory of epidemics*. London, Griffin.
 Bartlett, M. S. (1955) *An introduction to stochastic processes*. Cambridge University Press.
 Bartlett, M. S. (1960) *Stochastic population models in ecology and epidemiology*. London, Methuen.
 Daley, D. J., and Kendall, D. G. (1965) Stochastic rumours. *J. Inst. Math. Appl.* 1, 42.
 Fisher, R. A. (1922) On the dominance ratio. *Proc. roy. Soc. Edinb.* 42, 321.
 Fisher, R. A. (1936) The wave of advance of advantageous genes. *Ann. Eugen.* 7, 355.
 Galton, F. (1889) *Natural inheritance*. London, Macmillan.

- Kendall, D. G. (1949) Stochastic processes and population growth. *J. roy. statist. Soc. B* 11, 230.
- Kendall, D. G. (1951) Some problems in the theory of queues. *J. roy. statist. Soc. B* 13, 151.
- Kendall, D. G. (1952) Les processus de croissance en biologie. *Ann. de l'Inst. Henri Poincaré* 13, 43.
- Kendall, D. G. (1956) Deterministic and stochastic epidemics in closed populations. In: *Proceedings of the Third Berkeley Symposium on Mathematical Statistics and Probability*, IV, p. 149.
- Kernack, W. O. and McKendrick, A. G. (1927) A contribution to the mathematical theory of epidemics. *Proc. roy. Soc. A* 115, 700.
- Kolmogorov, A. N., Petrovsky, I., and Piskunov, N. (1937) Étude de l'équation de la diffusion avec croissance de la quantité de matière et son application à un problème biologique. *Bull. de l'Univ. d'Etat à Moscou (Sér. Intern.)* Sect. A, 1, fasc. 6, 1.
- McKendrick, A. G. (1926) Applications of mathematics to medical problems. *Proc. Edinb. math. Soc.* 44, 1.
- White, P. (1952) Certain non-linear models of population and epidemic theory. *Skand. Aktuar. Tidskr.* 35, 211.
- White, P. (1955) The outcome of a stochastic epidemic—a note on Bailey's paper. *Biometrika* 42, 116.

DISCUSSION

Dr O. M. LDWELL said that he wanted to make a few general remarks on the type of work discussed by Professor Kendall. He felt that its relevance to field epidemiology was not always obvious. The amount of information available differed from that available in other fields that had been discussed at the Conference and was limited to such facts as the number of cases that occurred in a time sequence (the rise and fall of the epidemic wave). But the epidemic arose from a complex situation with many variables. A sense of irrelevance and frustration could arise from this since, although it was not difficult to fit a mathematical representation to the observed facts, when the model had been set up it was difficult to decide whether it had any relationship to the real state of affairs.

Two approaches to the problem were possible. The first, which had been described by Professor Kendall, was synthetic: a hypothetical model was set up and comparison drawn with the observed facts. The mathematics might be complicated but this could be overcome by the use of Monte Carlo methods or of computers. This had been particularly useful in the stochastic approach to infections in small groups like the family. The second approach was analytical in that the data were not matched to a previous hypothesis; the pattern of the disease was related to factors in the individual or in the environment. This method was particularly applicable when infections occurred in a seasonal pattern for no known reason. In this connection, he quoted the work of Dr Spicer on the spread of poliomyelitis epidemics in different seasons and the way in which the size of epidemics varied. It was not so easy to continue this study on poliomyelitis since the widespread use of vaccine had virtually put an end to epidemics of this disease.

Dr Lidwell went on to say that in his own work he was concerned with applying this method to the study of the seasonal incidence of the common cold. He would like to know more from Professor Kendall about the application of stochastic methods to studies of infections in small linked groups.

Dr N. T. J. BAILEY congratulated Professor Kendall on an extremely lucid introduction to work on the theory of epidemics. He felt that it was important to note that there were two complementary approaches to this subject. Firstly,

there was the general study of large-scale phenomena, as discussed by Professor Kendall, which provided insight into the general properties of epidemic processes, such as threshold effects. Secondly, studies could be made of epidemics in small family groups, as mentioned by Dr Lidwell. In the latter case it was possible to investigate more precise biological models. For example, we could study the lengths of latent and infectious periods with regard to their statistical distributions, and actually estimate parameters of fundamental biological significance. The two types of study needed to be more carefully related, and considerable benefits could well result. Public health authorities would have more information on the contact and removal rates, for example, whilst general practitioners would be better able to advise patients about the length of the infectious period and tell them when it would be reasonably safe for them to go out in public again. Dr Bailey felt that many advances along these lines would be possible in this field.

SIR EDWARD COLLINGWOOD asked whether a linear model such as that described by Professor Kendall could be applied to vector-borne infections. He cited the example of the spread of myxomatosis among rabbits in Australia where the infection followed the rivers because the vector was the mosquito. He wondered whether complications might arise from infection in both directions, and in instances where removal was only by death as in the spread of myxomatosis.

PROFESSOR KENDALL in reply said that he liked Sir Edward's point about the rabbit and the river. The model already included the possibility of 'infection back'.

In reply to the point that had been raised concerning linked small groups he referred those who were interested in this topic to a paper by Rushton and Mautner (1955)* which dealt with this subject.

*Rushton, S., and Mautner, A. J. (1955) The deterministic model of a simple epidemic for more than one community. *Biometrika* 42, 126.