MATHEMATICAL MODELS IN EPIDEMIOLOGY

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Contents

Summary

This paper provides an overview of the use of mathematical models to explain the epidemiology of infectious diseases, and to assess the potential benefits of proposed control strategies. The development is broadly historical: beginning with the concept of mass action and compartmental models; proceeding through models for vector-born infections with special reference to malaria; touching on ideas arising in modelling the

population dynamics of macroparasites; and concluding with an examination of techniques for modelling transmission dynamics in structured populations. The treatment is deterministic throughout, some references for stochastic models are provided in the bibliography.

1. Models for Infectious Diseases

1.1 Historical Introduction

The diseases that motivated the development of modern epidemiological theory are arguably those due to childhood infections, most notably measles. This arose predominantly from their large public health importance in the late 19th and early 20th century. In late 19th century England a sophisticated system of vital statistics had been initiated by William Farr, and data series relating to several childhood infections became available that were both reliable enough and long enough to generate hypotheses about the mechanisms underlying epidemic spread. It was only at this time that the germ theory of infection - the notion that certain infections are caused by living organisms multiplying within the host and capable of being transmitted between hosts - became firmly established, due to the work of Pasteur and others.

The most striking aspect of measles epidemics, i.e. their regular cyclic behavior, was noticed first by Arthur Ransome around 1880. Speculation about the underlying cause centered on the availability of sufficiently many susceptible individuals of the right age-class in close enough proximity to each other, hence precursory ideas of critical community sizes for sustaining endemic measles were present. Two factors that commonly occur in many current models to investigate epidemic spread of measles and other infections are the age-structure of the population and the periodicity in *contacts*. The age and school season were recognized as important as early as 1896. William Hamer published a discrete time epidemic "model" for the transmission of measles in 1906. His observation can be reformulated as stating that the *incidence* of new cases in a time interval is proportional to the product *SI* of the (spatial) density *S* of *susceptibles* and the (spatial) density *I* of *infectives* in the population. This assumption of *mass action* - in analogy to its origin in chemical reaction kinetics – is fundamental to the modern theory of deterministic epidemic modelling. The popularity of mass action is explained by its mathematical convenience and the fact that at low population densities it is a reasonable approximation of a much more complex *contact process*.

1.2 The Concept of Mass Action

The state variables in an epidemiological model correctly refer to population density rather than population size. Where the population is confined to a fixed area this distinction has no consequence. Consider a single *susceptible* individual in a homogeneously mixing population. This individual contacts other members of the population at the rate C (with units time^{-1}) and a proportion I/N of these contacts are with individuals who are infectious. If the probability of transmission of infection given contact is β, then the rate at which the infection is transmitted to *susceptibles* is $\beta CI/N$, and the rate at which the *susceptible* population becomes *infected* is $\beta CSI/N$.

The *contact rate* is often a function of population density, reflecting the fact that contacts take time and saturation occurs. One can envisage situations where C could be approximately proportional to N (which corresponds to mass action), and other situations where C may be approximately constant. Hence terms like βSI and $\beta SI/N$ are frequently seen in the literature. For these, and in many instances where the population density is constant, the contact rate function C has been subsumed into β, which is now no longer a probability but a "transmission coefficient" with units time^{-1}.

1.3 The Size of an Epidemic

Consider an epidemic that occurs on a timescale that is much shorter than that of the population, in other words regard the population as having a constant size and ignore births and deaths. Assume that upon recovery the individual remains immune. At any time the population consists of S *susceptible* individuals, I *infected* and R immune (*removed*). A simple model that describes the changes in these numbers with time is

$$\frac{dS}{dt} = -\beta C \frac{SI}{N} \tag{1}$$

$$\frac{dI}{dt} = \beta C \frac{SI}{N} - \gamma I \tag{2}$$

$$\frac{dR}{dt} = \gamma I \tag{3}$$

The total size of the population, $N = S + I + R$ is constant, and one of the above equations is redundant, as any two specify the third. Any steady state solution ($S(t) = S^*$, $I(t) = I^*$, $R(t) = R^*$, $\forall t$) of equations (1 – 3) requires $I^* = 0$, hence this model does not admit an endemic equilibrium with infection present.

Now consider the passage of an epidemic through the population. Dividing equation (2) by equation (1) leads to

$$\frac{dI}{dS} = \frac{\gamma N}{\beta CS} - 1 \tag{4}$$

which may be integrated to obtain

$$I + S - \frac{\gamma N}{\beta C} \ln S = \text{constant} \tag{5}$$

Let the whole population be *susceptible* up to time zero, at which time a relatively small number I_0 become *infected*. Hence $S(0) = S_0 = N - I_0$ and $R(0) = 0$. Following the passage of an epidemic $\lim_{t \to \infty} I(t) = 0$, $\lim_{t \to \infty} S(t) = S_\infty$, and the number that have been *infected* (final size of the epidemic) is $S_0 - S_\infty$. These quantities satisfy the relationship

$$\ln\frac{S_\infty}{S_0} = \frac{\beta C}{\gamma}\left(\frac{S_\infty - S_0 - I_0}{N}\right) \tag{6}$$

Since the initial infection was small, $I_0 \downarrow 0$, and $S_0 \uparrow N$. Hence the proportion of the population that remains *susceptible* following the epidemic may be calculated from the so-called final size equation,

$$\ln\frac{S_\infty}{S_0} = \frac{\beta C}{\gamma}\left(\frac{S_\infty}{N} - 1\right) \tag{7}$$

Equation (7) has the solution $S_\infty = N$ (no epidemic) and another solution for S_∞ in the interval $(0, N)$ if and only if $\beta C > \gamma$. Hence, in biological terms, a small introduction of infection to the population would create an epidemic if the *basic reproduction ratio* ($R_0 = \beta C/\gamma$) is greater than one.

1.4 Compartmental Models

A compartmental model is one for which the individuals in a population are classified into compartments depending on their status with regard to the infection under study. They are usually classified by a string of letters that provides information about the model structure. For example, the model specified by equations $(1 – 3)$ would be called an *SIR* model, a compartmental model for infection transmission with an *exposed* (or latent) compartment (explicitly containing those infected but not yet infectious) and lasting immunity would be called an *SEIR* model, and situations where susceptibility can return after infection (or after immunity) would be called an *SIS* (or an *SIRS*) model.

An example of an *SEIR* model, analogous to that of the previous section, is

$$\frac{dS}{dt} = \mu N - \beta C\frac{SI}{N} - \mu S \tag{8}$$

$$\frac{dE}{dt} = \beta C\frac{SI}{N} - (\sigma + \mu)E \tag{9}$$

$$\frac{dI}{dt} = \sigma E - (\gamma + \mu)I \tag{10}$$

An equation for R is superfluous here since $N = S + E + I + R$ is constant. The model described by equations (8-10) is an extension of that described by equations (1-3), not only due to the introduction of an *exposed* class, but also because host births and deaths are explicitly included.

System (8-10) has two steady states. The first, where $S(t) = N$ and $E(t) = I(t) = 0$ for all t, corresponds to the situation with no infection present and the entire population

susceptible. The second

$$S(t) = S^* = \frac{(\sigma + \mu)(\gamma + \mu)N}{\sigma\beta C} \qquad (11)$$

$$E(t) = E^* = \frac{\gamma + \mu}{\sigma}I^* \qquad (12)$$

$$I(t) = I^* = \frac{\mu N}{\beta C}\left(\frac{N}{S^*} - 1\right) \qquad (13)$$

corresponds to an endemic steady state with constant numbers in the population *infected*. This is only biologically reasonable when $S^* < N$, that is when

$$R_0 = \frac{\sigma\beta C}{(\sigma + \mu)(\gamma + \mu)} > 1 \qquad (14)$$

where R_0 is the *basic reproduction ratio* of the infection.

The Jacobian matrix of system (8-10) is

$$J = \begin{pmatrix} -(\mu + \beta CI/N) & 0 & -\beta CS/N \\ \beta CI/N & -(\sigma + \mu) & \beta CS/N \\ 0 & \sigma & -(\gamma + \mu) \end{pmatrix} \qquad (15)$$

and local stability analysis determines that a steady state is stable when all eigenvalues of J have negative real parts when calculated using the steady state values for the dependent variables. Substituting the expressions for the steady states into equation (15) shows that the "no infection steady state" is stable when $R_0 < 1$, and the "endemic steady state" is stable whenever it exists, that is when $R_0 > 1$

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Bibliography

Anderson R.M. and May R.M. (1991). Infectious diseases of humans: dynamics and control. Oxford: Oxford University Press. [A comprehensive account of the subject at the time.]

Bartlett M.S. (1960). Stochastic population models in ecology and epidemiology. London: Methuen. [A useful and accessible treatment of stochastic models.]

Busenberg S. and Cooke K. (1993). Vertically transmitted diseases, models and dynamics. Berlin: Springer-Verlag. [A much more comprehensive treatment of mathematical epidemiology than would be inferred from the title.]

Daley D.J. and Gani J. (1999). Epidemic modelling: an introduction. Cambridge: Cambridge University Press. [A systematic treatment of stochastic models.]

Diekmann O. and Heesterbeek J.A.P. (2000). Mathematical epidemiology of infectious diseases: model building, analysis and interpretation. Chichester: Wiley. [The modern theory of epidemic models presented with numerous mathematical exercises and their solution.]

Grenfell B.T. and Dobson A.P., eds. (1995). Ecology of infectious diseases in natural populations. Cambridge: Cambridge University Press. [One of three volumes arising from the programme on epidemic models held at the Isaac Newton Institute for Mathematical Sciences at the University of Cambridge in 1993.]

Isham V.S. and Medley G.F., eds. (1996). Models for infectious human diseases: their structure and relation to data. Cambridge: Cambridge University Press. [One of three volumes arising from the programme on epidemic models held at the Isaac Newton Institute.]

Kermack W.O. and McKendrick A.G.. (1927). Contributions to the mathematical theory of epidemics. I. Proceedings of the Royal Society, Series A 115:700-721. (reprinted with parts II. and III. in Bulletin of Mathematical Biology, 53 (1991) 33-118). [The classic papers on epidemic models, they are often quoted but less often read.]

Mollison D, ed. (1996). Epidemic models, their structure and relation to data. Cambridge: Cambridge University Press. [One of three volumes arising from the programme on epidemic models held at the Isaac Newton Institute.]

Scott M.E. and Smith G., eds. (1994). Parasitic and infectious diseases: epidemiology and ecology. San Diego: Academic Press. [Written for non-mathematicians this book provides an accessible guide to the ideas.]

Biographical Sketch

Mick Roberts, graduated with a BSc in aeronautical engineering from Bristol University and an MSc in applicable mathematics from Cranfield Institute of Technology, before moving to New Zealand and completing a PhD in mathematics at Victoria University of Wellington. He was a scientist at AgResearch Wallaceville for more than 20 years, conducting research in the application of mathematical models to the epidemiology of infectious diseases and publishing more than eighty refereed articles in scientific journals and books. He is now Associate Professor of Mathematics at the Institute of Information and Mathematical Sciences, Massey University, Auckland.