16. Adachi, J. & Hasegawa, M. *MOLPHY: Programs for Molecular Phylogenetics 2.2* (Computer Science Monographs, No. 27, Institute of Statistical Mathematics, Tokyo, 1992).
17. Saccone, C., Lanave, C., Pesole, G. & Preparata, G. *Meth. Enzym.* **183,** 570–583 (1990).
18. Irwin, D. M., Kocher, T. D. & Wilson, A. C. *J. molec. Evol.* **32,** 128–144 (1991).
19. Arnason, U., Gullberg, A. & Widegren, B. *J. molec. Evol.* **33,** 556–568 (1991).
20. Graur, D. & Higgins, D. G. *Molec. Biol. Evol.* **11,** 357–364 (1994).
21. Krettek, A., Gullberg, A. & Arnason, U. *J. molec. Evol.* **41,** 952–957 (1995).
22. Saitou, N. & Nei, M. *Molec. Biol. Evol.* **4,** 406–425 (1987).
23. Arnason, U., Xu, X. & Gullberg, A. *J. molec. Evol.* **42,** 145–152 (1996).
24. Arnason, U. & Johnsson, E. *J. molec. Evol.* **34,** 493–505 (1992).
25. Arnason, U., Gullberg, A., Johnsson, E. & Ledje, C. *J. molec. Evol.* **37,** 323–330 (1993).
26. Xu, X. & Arnason, U. *Gene* **148,** 357–362 (1994).
27. Devereux, J., Haeberli, P. & Smithies, O. *Nucleic Acids Res.* **12,** 387–395 (1984).
28. Felsestein, J. *PHYLIP (Phylogeny Inference Package), Version 3.5c* (University of Washington, Seattle, 1993).

ACKNOWLEDGEMENTS. This work was supported by MURST (Italy), the Swedish Natural Sciences Research Council, and an EEC grant.

CORRESPONDENCE and requests for materials should be addressed to C.S. (e-mail: saccone@area.ba.cnr.it). Protein and nucleotide alignments analysed in the study are available on the World-Wide Web at http://www.ba.cnr.it/guineapig.html.

FIG. 1 *A*, Faroe Islands; *B*, Bornholm; *C*, Reykjavik (scaled). These are all ▶ examples of Bartlett's type III measles epidemic dynamics[12]. Top, monthly measles-case returns for each of the three communities. Between 1920 and 1970 the population of Reykjavik grew from 20,000 to 100,000, so we have scaled the incidence data per 25,000 of population. Middle, the distribution of epidemic event sizes. For the Faroes, $b \simeq 0.28$; for Bornholm, $b \simeq 0.28$; and for Reykjavik, $b \simeq 0.21$. Bottom, distribution of epidemic event durations. For the Faroe Island data, $c \simeq 0.8$; for Bornholm, $c \simeq 0.85$; and for Reykjavik, $c \simeq 0.62$. Clearly, scaling the measles incidence data will affect the epidemic sizes but leave the epidemic durations unscaled, hence this exponent is somewhat different from the Faroe and Bornholm cases. For each population, the exponents are unaffected by the specific choice of binning by decade.

Power laws governing epidemics in isolated populations

C. J. Rhodes & R. M. Anderson

Centre for the Epidemiology of Infectious Disease, Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, UK

TEMPORAL changes in the incidence of measles virus infection within large urban communities in the developed world have been the focus of much discussion in the context of the identification and analysis of nonlinear and chaotic patterns in biological time series[1–11]. In contrast, the measles records for small isolated island populations are highly irregular, because of frequent fade-outs of infection[12–14], and traditional analysis[15] does not yield useful insight. Here we use measurements of the distribution of epidemic sizes and duration to show that regularities in the dynamics of such systems do become apparent. Specifically, these biological systems are characterized by well-defined power laws in a manner reminiscent of other nonlinear, spatially extended dynamical systems in the physical sciences[16–19]. We further show that the observed power-law exponents are well described by a simple lattice-based model which reflects the social interaction between individual hosts.

Isolated island populations have often provided a valuable arena for the study of evolutionary and ecological processes because the subject of investigation is confined to a well-defined region of space that is well insulated from the influence of external factors. In the context of population studies, it is often possible in such settings to better observe effects that are intrinsic to the community without having to quantify the effect of peripheral populations.

The Faroe Islands (population 25,000) have extensive detailed measles-case returns (Fig. 1*A*, top). It is considered to be an accurate epidemiological data set because the population is small and localized. Also, because of the comparative rarity of measles outbreaks, few measles cases escape notice[20]. In the 58-year interval, there are 43 distinct epidemic events. An epidemic event is defined as the presence of a finite number of cases recorded in a sequence of consecutive months bounded by an absence of cases. An epidemic event has a duration, t, where $t = \tau_{\text{end}} - \tau_{\text{start}}$, τ_{start} is the month when cases in an event first appear, and τ_{end} is the next month when there are no more cases present. Similarly, an epidemic event has a size, s, where $s = \sum_{\tau_{\text{start}}}^{\tau_{\text{end}}} C(\tau)$, and $C(\tau)$ is the number of recorded cases of measles in the month τ.

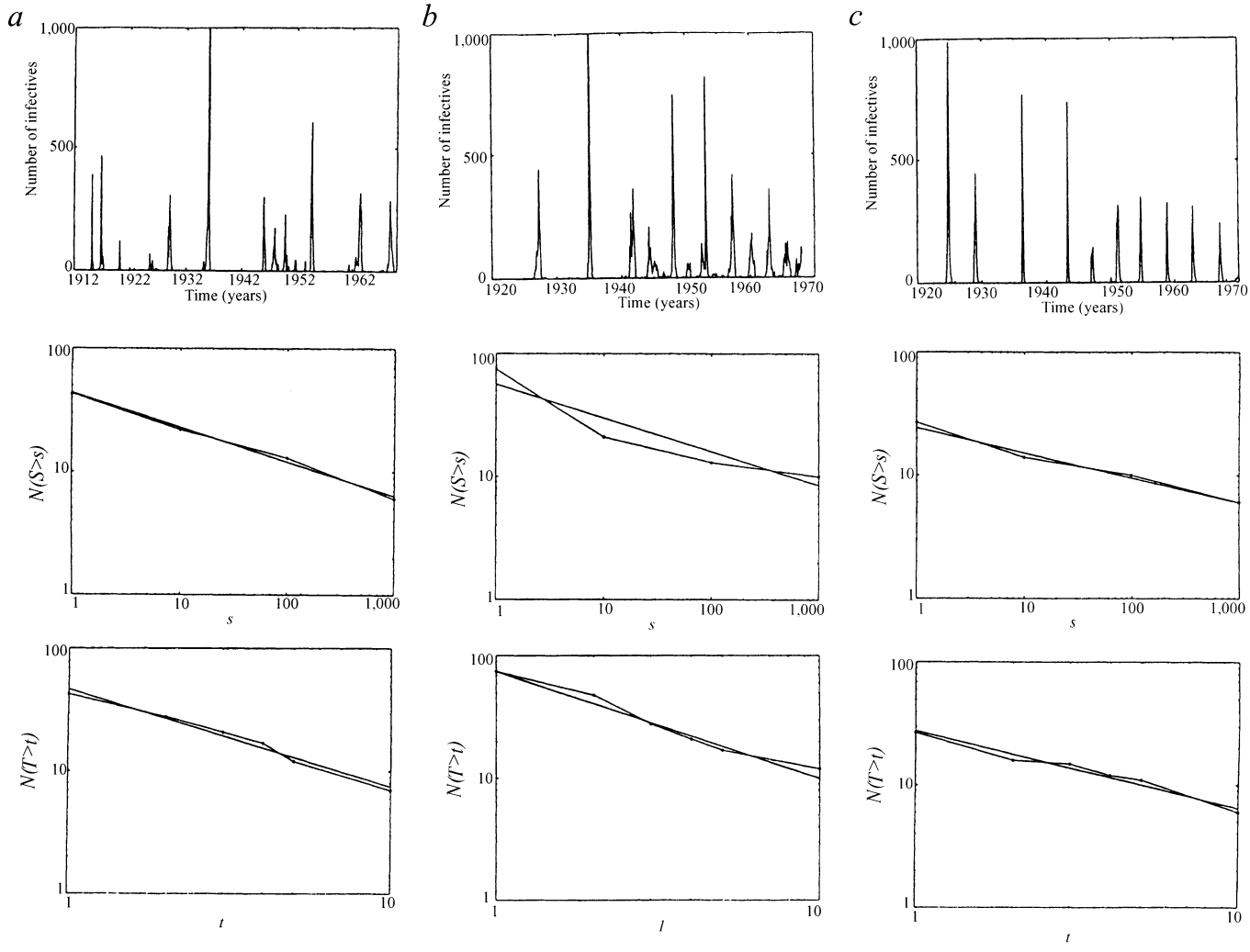
From Fig. 1*A*, top, it is apparent that there is no obvious discernible pattern to the dynamics; there is wide variation in both the duration and size of the epidemic events, reminiscent of the sort of dynamics observed in the study of earthquakes. In that case, the Gutenberg–Richter[21] law acts as an organizing principle connecting the frequency and magnitude of larger and smaller earthquakes. Performing the same analysis here, counting the number of epidemic events of size $>s$, there is a power-law dependence of the form $\log N(>s) = a - b\log(s)$. Thus, the number of epidemic events of size s scales as $N(s) \propto s^{-1-b}$, where $b \simeq 0.28$. The same analysis for the epidemic event durations indicates that the number of epidemics of duration t scales as $N(t) \propto t^{-1-c}$, where, from Fig. 1*A*, bottom, $c \simeq 0.8$. The presence of these scaling relations provides a useful way of estimating the likelihood, in a given interval of time, of epidemics of size s and duration t. Small short epidemics occur more often than large long epidemics, although their occurrence is connected and governed by the scaling exponents b and c. The exponents also apply to subportions of the data so, for example, we can use the epidemic distribution measured from the first half of the data set to predict the likely distribution of epidemic events in the second half.

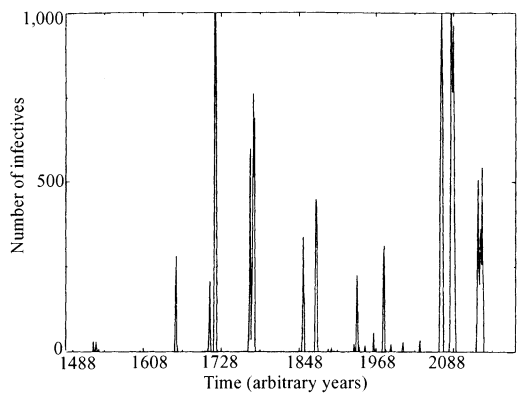
We have also applied this analysis to two other subendemic populations with extensive and accurate measles records, Bornholm and Reykjavik. Figure 1*B*, *C* indicates that the exponents, b and c, for all three populations are remarkably similar.

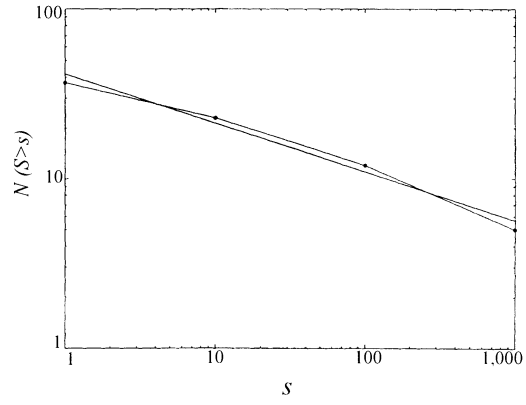
Mechanisms leading to the emergence of power laws of this sort are still not fully understood, although recently many spatially extended interacting model systems have been shown to exhibit similar behaviour. We use one such lattice-based model, previously used in discussion of 'forest-fire' dynamics[18,22,23], to provide a simple model for this phenomenon.

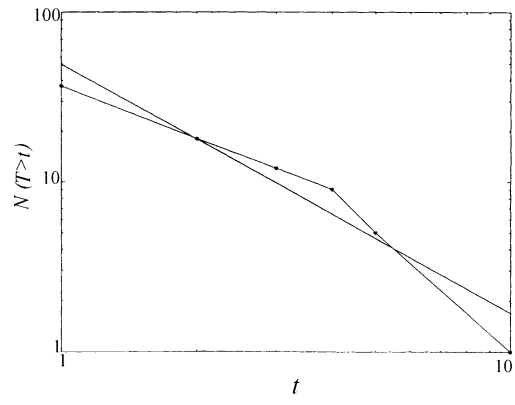
The dynamics of the model in Fig. 2 closely resemble those seen in the Faroe data. Exponents for the model data are similar to the actual epidemiological data; $b \simeq 0.29$ and $c \simeq 1.5$, with the simulation underestimating the number of long epidemics of more than 10 months duration. The connectedness of the spatial distribution of the population on the lattice seems to reflect the social networks that exist in real communities[24].

FIG. 2 Top left, time series of infectives for the model simulation. Each site in the $L \times L$ lattice is in one of three states: empty, occupied by a susceptible, or occupied by an infective. The lattice is updated synchronously at each time-step using the following rules: (1) susceptibles who are on nearest-neighbour sites to an infective become infective themselves; (2) infectives become inactive and the site they occupy becomes empty; (3) susceptibles are introduced onto empty lattice sites with a probability μ; (4) a new infective can arise when a susceptible is spontaneously infected with a probability ν. This effectively corresponds to an immigration term, whereby our lattice population is subject to infrequent infection from external sources. Periodic boundary conditions are used. These rules define a simple spatial *S-I* model. It is the simplest possible model of epidemic spread on a lattice and is, at best, a caricature of the known epidemiological processes. The lattice is 250×250, with $\mu = 0.000026$ and $\nu = \mu/300$.

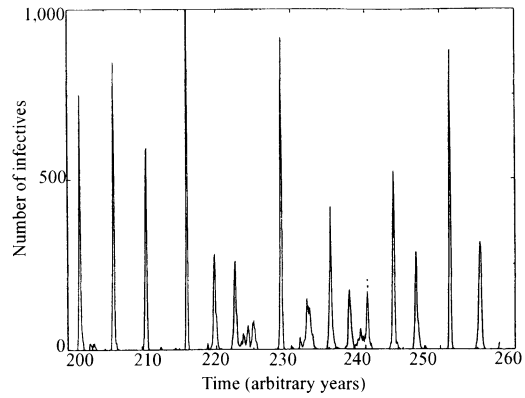


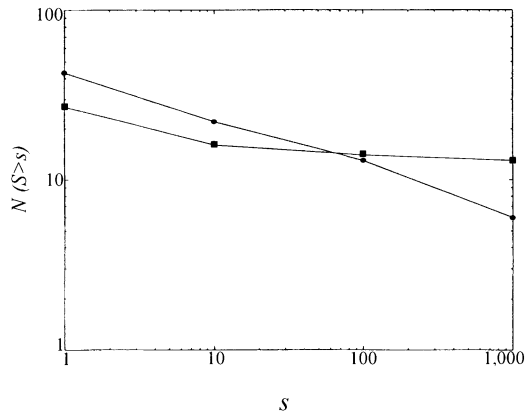






Mean population density on the lattice is 25,000. At equilibrium, with an average life expectancy of 70 years, we expect ~1 new susceptible to appear each day. The 43 epidemic events in 58 years sets a lower limit of $\nu/\mu \approx 1/400$, although we use $\nu/\mu \approx 1/300$ for the simulations. Birth of new susceptibles and immigration of infectives onto the lattice are modelled as Poisson processes, with a mean of 1 new susceptible appearing on the lattice at each time-step and a mean of one infective immigrating every 300 time-steps. Thus 1 time-step can be equated with one day. The *x*-axis is labelled for 696 arbitrary months (58 years). Top right, distribution of epidemic event sizes for the simulation data, $b \simeq 0.29$. Bottom, distribution of epidemic event durations for the simulation data, $c \simeq 1.5$. The exponent is severely affected by the poor prediction of long epidemics >10 months, but comparison with Fig. 1*A*, bottom, shows the simulation makes a good prediction of the distribution of epidemics of up to 5 months duration for the Faroes.





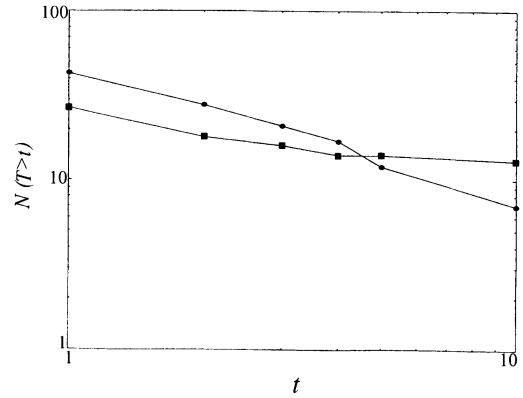


FIG. 3 Top left, time series of monthly number of infectives; bottom left, distribution of epidemic sizes (squares); and top right, epidemic duration (squares) for a stochastic Monte Carlo implementation of an SEIR model of measles in the Faroe Island population. The scaling for the Faroe Island (circles) data from Fig. 1 is shown for comparison. A constant population of 25,000 is used with a life expectancy of 50 years. The incubation and infectious intervals of measles are taken to be 7 days. R_0 is chosen to be 11. All births are into the susceptible class, with natural mortality occurring from each of the four classes. There is a Poisson influx of infectives into the community, on average every 300 days, as in the lattice simulation. The transients of the system are run off before data are recorded. No seasonality in the contact rate is used in these graphs, but it is found that inclusion of a sinusoidal seasonal driving term in the contact rate does not improve agreement between the model and the observed scaling.

For comparison, we illustrate the dynamics generated by a conventional stochastic SEIR model[3,7,8] of the Faroe Islands. Conventional measles parameters are used and the population is modelled as a single homogeneously mixing community, with the same low-level immigration rate of external infectives. As before, we calculate the distribution of epidemic sizes and durations (Fig. 3). The resulting times series of infectives looks similar to the observed island dynamics, but this calculation overestimates the number of larger epidemics and is not able to fit the observed data as well as the lattice model. The assumption of homogeneous mixing of susceptibles with infectives that underlie the SEIR equations appear to break down for small populations with infrequent epidemics. The replenishment of susceptibles onto vacant lattice sites and the nearest-neighbour contact spread of infection are central to reproducing the observed epidemic dynamics.

Our results suggest the existence of scaling laws for the size and duration of epidemics in the isolated island measles data sets. This places the dynamics of these epidemics in the same class as other spatially extended nonlinear dynamical systems, where scaling is also observed. In practice, this facilitates a form of prediction in which we can calculate the frequency of occurrence of epidemics of given size and duration. A simple spatial model generates almost the same exponents as are seen in our data analysis. The power-law phenomenon is also likely to be of relevance in the study of infrequent outbreaks of measles in highly vaccinated communities and in isolated rural populations in developing countries. The methods discussed here are completely general and could be applied to any other times series of communicable disease outbreaks in a small population. □

Received 9 February; accepted 11 April 1996.

1. May, R. M. *Nature* **261,** 459–467 (1967).
2. May, R. M. *Proc. R. Soc. Lond.* A **413,** 27–44 (1987).
3. Grenfell, B. T. *J. R. statist. Soc. B* **54,** 383–398 (1992).
4. Grenfell, B. T., Kleczkowski, A., Ellner, S. & Bolker, B. M. *Phil. Trans. R. Soc. Lond.* A **348,** 515–530 (1994).
5. Bolker, B. M. & Grenfell, B. T. *Proc. R. Soc. Lond.* B **251,** 75–81 (1993).
6. Grenfell, B. T., Bolker, B. M. & Kleczkowski, A. *Proc. R. Soc. Lond.* B **259,** 97–103 (1995).
7. Olsen, L. F., Truty, G. L. & Schaffer, W. M. *Theor. Pop. Biol.* **33,** 344–370 (1988).
8. Olsen, L. F. & Schaffer, W. M. *Science* **249,** 499–504 (1990).
9. Sugihara, G. & May, R. M. *Nature* **344,** 734–741 (1990).
10. Sugihara, G., Grenfell, B. & May, R. M. *Phil. Trans. R. Soc. Lond.* B **330,** 235–251 (1990).
11. Tidd, C. W., Olsen, L. F. & Schaffer, W. M. *Proc. R. Soc. Lond.* B **254,** 257–273 (1993).
12. Bartlett, M. S. *J. R. statist. Soc. A* **120,** 48–70 (1957).
13. Bartlett, M. S. *J. R. statist. Soc. A* **123,** 37–44 (1960).
14. Black, F. L. *J. theor. Biol.* **11,** 207–211 (1966).
15. Anderson, R. M. & May, R. M. *Infectious Diseases of Humans, Dynamics and Control* (Oxford Univ. Press, 1991).
16. Bak, P., Tang, C. & Weisenfeld, K. S. *Phys. Rev. A* **38,** 364–374 (1988).
17. Chen, K., Bak, P. & Obukhov, S. P. *Phys. Rev. A* **43,** 620–635 (1991).
18. Clar, S., Drossel, B. & Schwabl, F. *Phys. Rev. E* **50,** 1009–1018 (1994).
19. Sornette, A. & Sornette, D. *Europhys. Lett.* **9,** 197–202 (1989).
20. Cliff, A. D., Haggett, P. & Smallman-Raynor, M. *Measles. An Historical Geography of a Major Human Viral Disease from Global Expansion to Local Retreat 1840–1990* (Blackwell, Oxford, 1993).
21. Gutenberg, B. & Richter, C. F. *Ann. Geofis.* **9,** 1–10 (1956).
22. Bak, P., Chen, K. & Tang, C. *Phys. Lett. A* **147,** 297–300 (1990).
23. Drossel, B. & Schwabl, F. *Phys. Rev. Lett.* **69,** 1629–1632 (1992).
24. Ferguson, N., May, R. M. & Anderson, R. M. in *Spatial Ecology: The Role of Space in Population Dynamics and Interspecific Interactions* (eds Tilman, D. & Kareiva, P.) (Princeton Monographs in Population Biology, in the press).

ACKNOWLEDGEMENTS. We thank L. F. Olsen of Odense University for use of the Faroe Island and Bornholm measles data, A. D. Cliff of Cambridge University of use of the Iceland and Reykjavik measles data, and N. Ferguson of Oxford University for many useful discussions. Research support for C.J.R. and R.M.A. is provided by the Wellcome Trust.

CORRESPONDENCE should be addressed to C.J.R. (e-mail: chris.rhodes@zoology.oxford.ac.uk).