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Statistical mechanical considerations in the theory of the spread of the Hantavirus

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Abstract

Calculations in the theory of the spread of epidemics are described with particular focus on the estimation of motion parameters describing rodents that are the carriers of the Hantavirus epidemic. The data considered are of the "mark-recapture" kind, i.e., those collected by capturing, tagging and recapturing the animals in a prescribed finite region of space. The theoretical tool used is the Fokker–Planck equation, its characteristic quantities being the diffusion constant which describes the motion of the rodents, and the attractive potential which addresses their tendency to live near their burrows. The measurements are addressed through simple analytical calculations of the mean squared displacement of the animals relevant to the specific probing window in space corresponding to the trapping region. A Fourier prescription is provided to extract the home range of the animals from the observations. Applications of the theory to rodent movement in Panama and New Mexico are mentioned and several on-going generalizations of current models of Hantavirus epidemic spread are introduced.

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1. Introduction

The study of the spread of epidemics is important from multiple points of view. Health concerns constitute an obvious reason for carrying out such studies. A general understanding of spatially resolved interacting systems on a macroscopic scale is another. Among the epidemics we have studied, the Hantavirus appears especially convenient for starting one's investigations into the subject because of its simplicity from the conceptual viewpoint. We refer the reader to [1–6] for details and state here only the following essential features of Hantavirus which shape the modeling activity.

The Hantavirus infection is carried by mice that move from location to location, and is transmitted to other mice through what are probably aggressive encounters. The mice do not die, nor are otherwise impaired, from contraction of the virus. There is no "vertical transmission" of the disease, i.e., there are no mice born infected. Humans get the virus from the mice but have no feedback effects on the mice in the infection process. A simple model which can be constructed from these four features to describe the time evolution of the mice populations M_s (susceptible) and M_i (infected) is

$$\frac{\partial M_s}{\partial t} = b(M_s + M_i) - cM_s - \frac{M_s(M_s + M_i)}{K(x,t)} - aM_sM_i + D\nabla^2 M_s\,,$$
$$\frac{\partial M_i}{\partial t} = -cM_i - \frac{M_i(M_s + M_i)}{K(x,t)} + aM_sM_i + D\nabla^2 M_i\,. \tag{1}$$

For the sake of simplicity, all parameters except K are considered to be independent of time t and space x, and detailed considerations such as those arising from gender and age of the animals are neglected. The meaning of the parameters will be explained below. This simple model may be regarded from the ecological viewpoint as a so-called SI model extended to include spatial resolution and diffusive transport, and from the mathematical point of view as a system obeying the Fisher equation [7] with internal states representing infection or its absence, respectively. While near-trivial to conceive, this model has had considerable success in the short time since it was proposed for the Hantavirus [3]. It has led to qualitative and semi-quantitative success in explaining observations such as spatio-temporal patterns in the epidemics. These patterns are associated with correlations between periods of precipitation and epidemic outbreaks, and with the spatial location of refugia–regions of the landscape in which infection persists during off-periods of the epidemic [3,5]. Other applications of the model include the detailed understanding and control of traveling waves of infection [4], fluctuations arising from the finiteness of the numbers and discreteness of the population of the rodents [8,9], environmental effects [10], curious switching effects that have been predicted to occur [11], and extensions to unrelated systems such as bacteria in Petri dishes [12,13]. This success of, and explosion of interest in, the so-called AK model represented by Eq. (1), naturally suggests that one should devise practical prescriptions for the extraction of the parameters constituting the

model from measurements in the field. This is the subject of the analysis in the next section.

2. Extraction of D and the interplay of length scales

The importance of the quantitative extraction of the parameters in (1), followed, if necessary, by generalizations of the model to incorporate additional structure inherent in the animal dynamics, is clear from the above discussion. Let us focus here on the former, i.e., the process of the extraction of the parameters. The parameters may be listed as a, b, c, K and D. It turns out that observational collection of data concerning the aggression rate a, through which infection is thought to be transmitted during mouse–mouse encounters, is so difficult that, at least at the present moment, it must be considered an adjustable parameter. The mouse birth rate b and the death rate c are obtained from field observations without too much trouble, although there are several subtleties involved that we do not describe here for reasons of space. With some effort, reasonable estimates of the environment resource parameter $K(x, t)$ as a function of location and time can be obtained by counting food (such as nuts and water) available to the mice in the different locations, as well as by acquiring aerial photographs of the vegetation cover. Relative, rather than absolute, quantification of K is possible in this way. In some ways the most important parameter in the list given above is the mouse diffusion constant D since the assumed mechanism for the spread of the epidemic is the diffusion (movement) of infected mice over the terrain followed by the transmission of infection to susceptible mice. If one makes the simple assumption that mouse movement is a random walk, it appears straightforward to measure D from records of the movement through the use of the well-known proportionality of the mean squared displacement (msd) to Dt. Careful examination of extensive mark-recapture data for mice in Panama and New Mexico lead one to deduce D directly in this manner [14,15]. However, the mouse msd, which grows linearly with t for short times, is found to *saturate* at large times. One way of explaining this (perhaps) surprising appearance of a length scale in the random movements of the mice is to ascribe it to the fact that animals typically move near fixed locations (burrows) for reasons of food and security [16–18]. However, there is another, quite prosaic, explanation: that the saturation could be arising merely from the fact that mark-recapture observations employ a limited region of space where the traps are laid out. It is possible to show analytically [14] that either of these factors could independently lead to the saturation of the mean squared displacement. It is crucial, therefore, to investigate deeper into the interplay of these two length scales.

3. Disentangling the length scales via a Fourier prescription

To disentangle these two sources of the observed saturation is an important undertaking. Let us begin by assuming that the movement of each mouse follows a

Fokker–Planck equation for the mouse probability distribution $\mathscr{P}(x,t)$:

$$\frac{\partial \mathscr{P}(x,t)}{\partial t} = \frac{\partial}{\partial x}\left[\frac{\mathrm{d}U(x)}{\mathrm{d}x}\,\mathscr{P}(x,t)\right] + D\frac{\partial^2 \mathscr{P}(x,t)}{\partial x^2}\,, \tag{2}$$

wherein $U(x)$, the potential under the action of which the animal is forced to roam, describes the reduced randomness of the walk associated with the tendency to stay near the burrow. A pure random walk, as in a simple diffusive process in the AK model (1), has $U(x)=0$. When $U(x)\neq 0$ we will identify its characteristic length with the home range of the animal which we will denote by L. We restrict our analysis here to one dimension for simplicity.

It is clear that msd saturation may arise from the appearance of the finite length L associated with $U(x)$, the home range. But it may also arise from the finite "grid length" G over which the mice are captured (at positions that we will call x_0) and recaptured (at positions that we will call x). Let us also keep in mind that the observables must be calculated for multiple mice that have their home burrows located at multiple positions x_c. If the density of these burrow locations is $\rho(x_c)$, the combined expression for the saturation value of the msd, denoted by $\overline{\Delta x^2_{ss}}$, is

$$\overline{\Delta x^2_{ss}} = \frac{\int_{-\infty}^{\infty}\mathrm{d}x_c\rho(x_c)\int_{-G/2}^{G/2}\mathrm{d}x_0\int_{-G/2}^{G/2}\mathrm{d}x\,(x-x_0)^2\mathrm{e}^{-\frac{U(x_0-x_c)+U(x-x_c)}{D}}}{\int_{-\infty}^{\infty}\mathrm{d}x_c\rho(x_c)\int_{-G/2}^{G/2}\mathrm{d}x_0\int_{-G/2}^{G/2}\mathrm{d}x\,\mathrm{e}^{-\frac{U(x_0-x_c)+U(x-x_c)}{D}}}\,. \tag{3}$$

In writing (3), advantage has been taken of the steady-state solution of the Fokker–Planck equation, well-known [19] in statistical mechanics to be the appropriately normalized exponential of the potential $U(x-x_c)$. By reexpressing the quantities in the right-hand side of (3) in terms of Fourier transforms and exploiting the relation between moments in real space and derivatives in reciprocal space, the right-hand side of (3) can be recast in the form of convolution integrals in reciprocal space. If the distribution of the burrow locations, $\rho(x_c)$, is taken to be uniform over the terrain, the convolutions disappear and (3) yields the compact formula

$$\overline{\Delta x^2_{ss}} = -\frac{\int_{-\infty}^{\infty}\mathrm{d}k\frac{\partial^2\hat{P}^2(k)}{\partial k^2}\frac{[1-\cos(Gk)]}{k^2}}{\int_{-\infty}^{\infty}\mathrm{d}k\hat{P}^2(k)\frac{[1-\cos(Gk)]}{k^2}}\,. \tag{4}$$

This result expresses the msd as a ratio of two single integrals over reciprocal space. Each integrand is a product of two conceptually separated factors: a *probe function* determined solely by the grid size G (independently of mice characteristics) and a *mouse motion quantity* determined solely by the mouse motion characteristics $U(x)$ and D (independent of the probe, i.e., the grid size). In (4), k spans the space reciprocal to real space in which the mouse moves, and $\hat{P}(k)$ is the Fourier transform of $\exp[-U(x)/D]$. The probe function is $(1-\cos Gk)/k^2$. The mouse motion factor is the square of the Fourier transform of $\exp[-U(x)/D]$ in the denominator, and its second k-derivative in the numerator. The home range L is naturally

defined as

$$L^2 = -2\left.\frac{\frac{\partial^2 \widehat{P}(k)}{\partial k^2}}{\widehat{P}(k)}\right|_{k=0}.$$

It can be obtained from the saturation value of the observed mean squared displacement by combining its definition with (4) and using the fact that G, the size of the trap region, is known.

The practical prescription provided by this analysis works as follows. For specific assumed forms of the confining potential $U(x)$, the sigmoidal curve of the dependence of the saturation value of the mean squared displacement $\overline{\Delta x^2_{ss}}$ (expressed in terms of the square of the known grid size) is plotted against the ratio $\zeta = L/G$ from the analytic Fourier expression (4). The observed value of the ordinate allows one to read off the value of $\zeta = L/G$ as shown. Since G is known, L is obtained directly. The disentangling of the two length scales is thus complete.

Giuggioli et al. [14] and Abramson et al. [15] have deduced explicit values of the home ranges of two different kind of mice in Panama and New Mexico respectively, through the application of this technique. The Fourier prescription provided here is a reformulation of the method underlying the analysis in Refs. [14,15]. The reader is referred to those papers for details and for the extracted values of the home range. A detailed theory of home range estimation may be found in the forthcoming paper by Giuggioli et al. [20].

4. Concluding remarks

We have described above a theoretical framework for the extraction of the motion parameters of mice moving diffusively within confining potentials, with focus on the problem of the determination of the home range size, and have provided a Fourier prescription to be used for arbitrary potentials. The prescription can be shown to be equivalent to a different procedure given by Giuggioli et al. [20]. An application of this prescription results in reasonable realistic extracted values of the home range size L for different type of mice in different environments: e.g., 60–90 m for *Zygodontomys brevicauda* in Panama and about 100 m for *Peromyscus maniculatus* in New Mexico. While having such quantitative information is the primary goal of the analysis, an immediate consequence, of even greater importance, is the impetus (indeed, necessity) to generalize the AK model expressed in (1) to incorporate home ranges. We have undertaken such investigations in a variety of ways and on multiple fronts. Space restrictions[1] permit only a brief sketch rather than a detailed description.

One simple way of incorporating home ranges in our model of epidemic spread is to add potential terms as in (2) to (1). Such analysis, carried out by MacInnis et al. [21] has resulted in substantial modification in the AK predictions for refugia sizes and shapes. A simpler model modification in the AK equations has led us [22] to deduce memory-possessing variations of the AK equations on the one hand and

[1]We mean space restrictions for the author in the journal, not for the mouse in the field.

time-dependent diffusion constant variations on the other. A particularly fertile model we have developed [23] considers the dynamics of two types of mice, stationary and itinerant (and susceptible and infected in each category). The stationary mice are the adults that move within their home ranges and do not stray far from the burrow. The itinerant mice are the subadults that must leave to find their own home ranges. Our studies, which employ a combination of nonlinear analysis and simulations, have led to unexpected new insights into the spread of the Hantavirus. These will be reported elsewhere.

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