

Basic modelling macroparasitic diseases

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Abstract

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1 Introduction

Mathematical models play an important role in understanding the transmission and impact of macroparasite infection control measures [2, 3, 19]. The first works on the theory of helminth infection was published in the 1960s by Tallis and Leyton by developing stochastic models of nematode parasite transmission in sheep and cattle [14, 17, 18].

Simultaneously Macdonald show that a consequence of sexual reproduction of distributed parasites within individual hosts was the inability to generate fertile infectious material when prevalence is low [15].

Anderson and May then introduced much more general descriptions of helminth population dynamics. They developed descriptions for a model based on host age, distribution of parasite numbers per host, density dependence of egg production, and sexual mating functions that depend on parasite distribution and reproductive habits [1, 2].

In this article we develop an analytical framework to describe the transmission dynamics of parasitic infections. We first analyzed the epidemiological patterns of these infections. We studied the individual distribution of the parasites in the community of hosts and also the distribution by sex of the parasites. From this we obtain expressions for the fertilized egg production and the mating probability of parasites. For these last variables we consider a density-dependent fecundity, a characteristic of helminth parasites.

Then we present the calculations of the equilibrium values of the model and the basic reproduction number R_0 defined for case of macroparasitos as the average number of new parasite offsprings caused by one typical parasite, from one generation to the next. We show that our model has a saddle node bifurcation. Finally we show all the analytical results supported by numerical analysis.

2 Epidemiological patterns

2.1 Distribution of parasite numbers per host

For macroparasites, the distributions are highly aggregated, such that most host harbour few parasites and a few host harbour the majority of the parasite population [7]. This implies that the variance in parasite burden per host is much greater in value than the mean burden.

The most used distribution is the negative binomial distribution which provide an accurate description of the observations [16]. The negative binomial distribution is a two parameters distribution, which usually are the mean parasite burden in the host population m and the inverse dispersion parameter k which is related with the degree of the over-dispersion [5]. Moreover, it can be shown that the limiting distribution of the $NB(m, k)$ distribution, as $k \rightarrow \infty$, is a Poisson distribution $Po(m)$. If W is a random variable, the number of parasites per host, the probability of observing n parasites per person, $P(W = n)$, for the negative binomial model is defined as

$$P(W = n) = \frac{\Gamma(k + n)}{\Gamma(n + 1)\Gamma(k)} \left(\frac{k}{m + k}\right)^k \left(\frac{m}{m + k}\right)^n \quad (1)$$

2.2 Distribution of parasites by sex

Many of parasitic infection are transmitted to their hosts most often through the ingestion of the larvae and eggs of intestinal parasites.

We assume that in the same event (ingestion of eggs or larvae) the host can acquire several parasites, which can be male or female.

Therefore we assume that the distribution of females or males must be a joint distribution.

We also assume that the ratio of females to males in the parasite population is 1:1. That is, if m is the mean of the distribution of parasites, the mean number of parasites females and males are given by $\frac{m}{2}$ and $\frac{m}{2}$ respectively.

Let W be a random variable, the number of parasites per host and F the number of female parasites per host. If we assume that $W \sim NB(m, k)$, then the case of the distribution of female parasites per host, is given by

$$\Pr(F = i) = \sum_{n \geq i} \binom{n}{i} 2^{-n} \Pr(W = n) \quad (2)$$

where $\Pr(W = n)$ is given by the expression (1) and $i, n - i$ is the number of female, male respectively in a host with n parasites.

2.3 Density-dependent fecundity

In population ecology, density-dependent processes occur when population growth rates are regulated by population density.

In macroparasites life cycles, density-dependent processes can influence parasite fecundity, establishment and survival within the host. In the case of helminth parasites, there is a density-dependent fecundity in which the weight of females and their egg production rates decrease as the parasite burden on the host increases [6, 20].

This negative density-dependence can be described mathematically by the negative exponential function

$$\lambda(n) = \lambda_0 \exp[-\gamma(n - 1)] \quad (3)$$

where $\lambda(n)$ is the per capita female fecundity within a host with a parasite burden of size n , λ_0 is the intrinsic fecundity in absence of density-dependence effects and γ is the density-dependence intensity. A study for *Ascaris lumbricoides* is presented in [11].

To simplify notation in rest of the text we will express the female fecundity by $\lambda(n) = \lambda_0 z^{n-1}$ where $z = e^{-\gamma}$.

2.4 Mean egg production per host

Due to the effects of density-dependent fecundity, the total egg production by females decreases as the parasite burden in host increases. Therefore, from the distribution of parasites per host, the mean egg production per host is given by the expression

$$\begin{aligned} \sum_{i \geq 0} i \lambda(n) \Pr(F = i) &= \sum_{i \geq 0} \sum_{n \geq i} i \lambda(n) \binom{n}{i} 2^{-n} \Pr(W = n) \\ &= \lambda_0 \sum_{n \geq 0} z^{n-1} \Pr(W = n) \sum_{i=0}^n i \binom{n}{i} 2^{-n} \\ &= \lambda_0 \frac{m}{2} \psi(m, k, z) \end{aligned} \quad (4)$$

where $i \lambda(n)$ is the egg production of i females, $\binom{n}{i} 2^{-n} \Pr(W = n)$ is the probability of having i females, both cases within a host with n parasites; and the term ψ is given by

$$\psi(m, k, z) = \left[1 + (1 - z) \frac{m}{k} \right]^{-(k+1)} \quad (5)$$

This last term is also known as the effective transmission contribution of the female population to the parasite reservoir (in the form of eggs or larvae) [6].

2.5 Mean fertilized egg production per host

For the fertilized egg production, we must consider only the fertilized females. Therefore the expression for the mean fertilized egg production is given by

$$\begin{aligned} \sum_{n \geq 1} \sum_{i=0}^{n-1} i \lambda(n) \binom{n}{i} 2^{-n} \Pr(W = n) &= \lambda_0 \frac{m}{2} \sum_{n \geq 0} n z^{n-1} \Pr(W = n) (1 - 2^{-n+1}) \\ &= \lambda_0 \frac{m}{2} \psi(m, k, z) \phi(m, k, z) \end{aligned} \quad (6)$$

where $i \lambda(n)$ is the egg production of i females, $\sum_{i=1}^{n-1} \Pr(W = n) \binom{n}{i} 2^{-n}$ is the probability of having at least one male in a burden of n parasites; and the term ϕ is given by

$$\phi(m, k, z) = 1 - \left[\frac{1 + \left(1 - \frac{z}{2}\right) \frac{m}{k}}{1 + (1 - z) \frac{m}{k}} \right]^{-(k+1)} \quad (7)$$

Note that the term ϕ is the fraction of eggs that are fertilized by male parasites. Therefore ϕ is the probability of fecundity of eggs or mating probability of female parasites.

3 A basic model

3.1 Model structure

The model presented in this paper is based on a model developed by Anderson and May [2, 4]. The conceptual framework of parasite transmission dynamics is conceptualized as a population of mature worms within human hosts and a population of infective stages of free life of these parasites (eggs and larvae) found in the environment (reservoir). Hosts can become infected by contact with the infective stages (eggs or larvae) and can contaminate the environment (reservoir) with infective stages (eggs and larvae).

The dynamic variables of our model are the mean parasite burden of the population, m , and the infectious environment formed by eggs and larvae of these parasites, ℓ . The model is defined as follows,

- Consider a community of human hosts of constant size N .
- Let $p_j(t)$ be the parasite burden of a host j and $m(t) = \frac{\sum_j^N p_j(t)}{N}$ the mean parasite burden in a community of size N at time t .

- Human hosts acquire parasites by ingesting their fertilized eggs or larvae, which are found in a common environment. Assuming that $\ell(t)$ is the reservoir of eggs or larvae in environment, the rate of contact or infection of a host j is β_j , and $\beta = \frac{\sum_j^N \beta_j}{N}$ the average infection rate per host.
- Suppose that humans die at a rate μ_h (killing worms inside), and that parasites die inside humans at a rate μ_p .
- Then an individual's parasite burden dynamics are described by the following equations:

$$\frac{dp_j}{dt} = \beta_j \ell - \mu_h p_j - \mu_p p_j \quad (8)$$

To obtain a more representative parasite burden dynamics of the host community, let's consider the mean parasite burden

$$\frac{dm}{dt} = \beta \ell - (\mu_h + \mu_p) m \quad (9)$$

- Now let's consider ℓ . The dynamics between the reservoir ℓ and a host j is given by $\rho_j e_j - \beta_j \ell$ where ρ_j is the contribution rate (to the reservoir) of a host j , $\rho = \sum_j^N \rho_j$ is the average contribution rate per host, and e_j is the fertilized egg production of a host j .
- Therefore, the dynamics between the reservoir ℓ and the mean parasite burden m is given by the following equation:

$$\frac{d\ell}{dt} = \rho N e - \mu_\ell \ell - \beta N \ell \quad (10)$$

where μ_ℓ is the mortality rate associated to ℓ and e is the mean fertilized egg production per host, obtained in the section 2.5 and is given by $e = \lambda_0 \frac{m}{2} \psi(m, k, z) \phi(m, k, z)$

This gives us the basic model for parasite transmission dynamics.

$$\frac{dm}{dt} = \beta \ell - (\mu_h + \mu_p) m \quad (11)$$

$$\frac{d\ell}{dt} = \frac{\rho N \lambda_0}{2} m \psi(m) \phi(m) - (\mu_\ell + \beta N) \ell \quad (12)$$

3.2 Equilibria and basic reproduction number

From the equation (12) we obtain that in equilibrium

$$\ell^* = \frac{\rho N \lambda_0}{2(\mu_\ell + \beta N)} m \psi(m) \phi(m) \quad (13)$$

and substituting (13) in the equation (11) we get the following equation for the dynamics of m

$$\frac{dm}{dt} = (\mu_h + \mu_p) [R_0 \psi(m) \phi(m) - 1] m \quad (14)$$

where the parameter R_0 is the basic reproductive number which, by definition, is independent of the effects of density-dependence and mating probability

$$R_0 = \frac{\rho N \lambda_0 \beta}{2(\mu_\ell + \beta N)(\mu_h + \mu_p)} \quad (15)$$

Therefore from the equation (14) we can obtain the equilibrium condition for the mean parasite burden

$$\psi(m^*; k, z) \phi(m^*; k, z) = 1/R_0 \quad (16)$$

By bifurcation analysis we obtain that the system of the equations (11) and (12) has a saddle node bifurcation at the point (m^*, R_0^*) where these values are given by

$$m^* = \frac{k \left(\frac{1-z/2}{1-z} \right)^{\frac{1}{k+2}} - k}{(z-1) \left(\frac{1-z/2}{1-z} \right)^{\frac{1}{k+2}} + (1-z/2)} \quad (17)$$

$$R_0^* = [\psi(m^*; k, z) \phi(m^*; k, z)]^{-1}$$

Due to the type of bifurcation present in the system, the solution of the equation (16) presents two solutions. The first is called **stable** and is the endemic solution of the system. This equilibrium is an attractor for a range of values of $R_0 > R_0^*$. The second is known as **unstable** since it corresponds to a repulsor in the phase plane, that is, a barrier where the values of $M(t)$ above it are attracted to the stable equilibrium and the values of $M(t)$ below are attracted to the extinction equilibrium $M^* = 0$, which is the trivial solution of the equation (14). **PONER REF LA FIGURA**

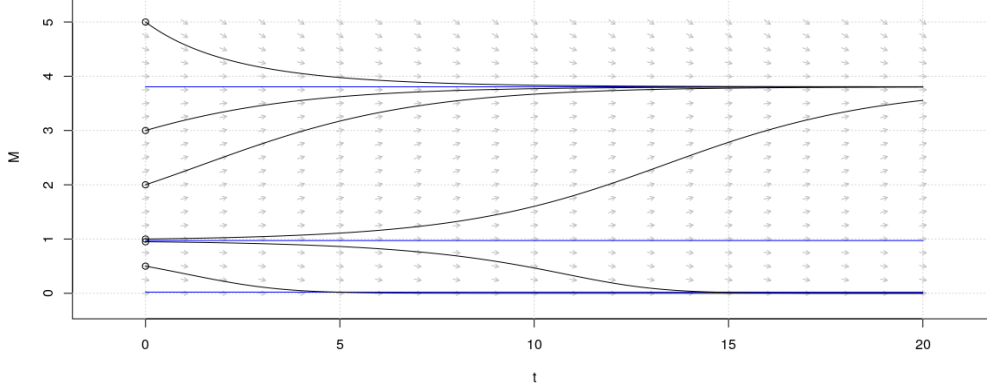


Figure 1

3.3 Saddle-node bifurcation

We will show that the basic model developed in the section 3.1 presents a saddle node bifurcation. To do this, let us consider the equation (14)

$$\frac{dm}{dt} = (\mu_h + \mu_p) [R_0 \psi(m) \phi(m) - 1] m$$

which we compactly denote by $\frac{dm}{dt} = f(m, R_0)$. A necessary condition for the existence of a saddle node bifurcation in (m^*, R_0^*) is

$$\begin{aligned} f(m^*, R_0^*) &= 0 \\ \frac{\partial f}{\partial m}(m^*, R_0^*) &= 0 \end{aligned} \tag{18}$$

where the first of these conditions is the equilibrium condition (16) of the system

$$\psi(m^*; k, z) \phi(m^*; k, z) = 1/R_0^*,$$

and so we get the following equilibrium condition for m^*

$$\frac{\partial}{\partial m} \psi(m^*; k, z) \phi(m^*; k, z) = 0 \tag{19}$$

The value of m corresponding to this last condition is

$$m^* = \frac{k \left(\frac{1-z/2}{1-z} \right)^{\frac{1}{k+2}} - k}{-(1-z) \left(\frac{1-z/2}{1-z} \right)^{\frac{1}{k+2}} + (1-z/2)} \tag{20}$$

and its corresponding basic reproductive number is

$$R_0^* = [\psi(m^*; z, k)\phi(m^*; z, k)]^{-1} \quad (21)$$

A sufficient condition for the existence of a saddle node bifurcation at (m^*, R_0^*) is

$$\begin{aligned} \frac{\partial f}{\partial R_0}(m^*, R_0^*) &\neq 0 \\ \frac{\partial^2 f}{\partial m^2}(m^*, R_0^*) &\neq 0 \end{aligned} \quad (22)$$

By a Taylor series expansion of the function f in a neighborhood of (m^*, R_0^*) , the equation (14) is left

$$\frac{dm}{dt} = f(m^*, R_0^*) + (m - m^*) \frac{\partial f}{\partial m} \Big|_{(m^*, R_0^*)} + (R_0 - R_0^*) \frac{\partial f}{\partial R_0} \Big|_{(m^*, R_0^*)} + \frac{1}{2} (m - m^*)^2 \frac{\partial^2 f}{\partial m^2} \Big|_{(m^*, R_0^*)} + \dots \quad (23)$$

Therefore locally at the point (m^*, R_0^*) the equation is of the form

$$\frac{dm}{dt} = \alpha(R_0 - R_0^*) + \beta(m - m^*)^2 \quad (24)$$

where the values $\alpha = (\mu_h + \mu_p) \frac{m^*}{R_0^*}$ and $\beta = (\mu_h + \mu_p) R_0 m^* \frac{\partial^2 F}{\partial m^2}(m^*)$ with $F(m) = \psi(m; z, k)\phi(m; z, k)$ which is the normal form of a saddle node bifurcation.

4 A heterogeneous model

In this section we will consider the most general and realistic case for a host population H . Unlike the homogeneous model presented in the previous section, here we present a model that accounts for host population heterogeneity, where subpopulations H_i (e.g., age groups, risk groups, [2, 3?]) have different infection risks. The dynamics of infection for the case of a heterogeneous population is described as follows

$$\begin{aligned} \frac{dm_i}{dt} &= \beta_i \ell - (\mu_h + \mu_p) m_i \\ \frac{d\ell}{dt} &= \frac{\lambda_0}{2} \sum_i \rho_i \pi_i m_i F(m_i) - (\mu_\ell + \sum_i \beta_i \pi_i) \ell \end{aligned} \quad (25)$$

where π_i is the portion of H to H_i such that $\sum_i \pi_i = 1$.

4.1 Equilibria and basic reproduction number

From the system (25) we obtain that in equilibrium

$$\ell^* = \frac{\lambda_0}{2(\mu_\ell + \sum_i \pi_i \beta_i)} \sum_i \rho_i \pi_i m_i F(m_i) \quad (26)$$

and substituting this in the rest of the equations of the initial system we obtain the following equation for the dynamics of the mean burden m_i of the subpopulation H_i of hosts

$$\frac{dm_i}{dt} = \beta_i \frac{\lambda_0}{2(\mu_\ell + \sum_j \pi_j \beta_j)} \sum_j \rho_j \pi_j m_j F(m_j) - (\mu_h + \mu_p) m_i \quad (27)$$

The mean burden m of the total host population $H = \bigcup_i H_i$ is given by

$$m = \sum_i \pi_i m_i \quad (28)$$

where π_i is the portion of the population H corresponding to the subpopulation H_i , and which is described by

$$\frac{dm}{dt} = \left(\sum_i \pi_i \beta_i \right) \frac{\lambda_0}{2(\mu_\ell + \sum_j \pi_j \beta_j)} \sum_j \rho_j \pi_j m_j F(m_j) - (\mu_h + \mu_p) m \quad (29)$$

From this equation, the equilibrium mean parasite burden, m^* , for the total population is given by

$$\sum_i \pi_i \frac{\lambda_0 \rho_i}{2(\mu_\ell + \sum_j \pi_j \beta_j)(\mu_h + \mu_p)} \left(\sum_j \pi_j \beta_j \right) F(m_i^*) m_i^* - m^* = 0 \quad (30)$$

This is not an explicit expression of the equilibria m_i^* . Therefore, the equilibrium value can only be solved numerically. An equilibrium condition for the mean burdens of each subpopulation H_i is given by

$$F(m_i^*) = 1/R_0^i \quad (31)$$

where we define by $R_0^i = \frac{\lambda_0 \rho_i}{2(\mu_\ell + \sum_j \pi_j \beta_j)(\mu_h + \mu_p)} \left(\sum_j \pi_j \beta_j \right)$ to the basic reproductive number of each subpopulation H_i which is the number of adult females that are born of a adult female from a host in subpopulation H_i in the absence the effects of density-dependence and the mating probability. For this

equilibrium situation, we obtain that the mean parasite burden of each sub-population H_i is given by $m_i^* = \frac{\beta_i}{\sum_j \pi_j \beta_j} m^*$. The general basic reproductive number R_0 for the total population is given by

$$R_0 = \frac{\lambda_0}{2(\mu_\ell + \sum_j \pi_j \beta_j)(\mu_h + \mu_p)} \sum_i \pi_i \rho_i \beta_i \quad (32)$$

where we assume the absence the effects of density-dependence and the mating probability [2], that is, we assume in the system (25) the function F equal to unity.

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Conflict of Interest

The authors have declared no conflict of interest.

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