Modeling macroparasite diseases dynamics

Modelado de la dinámica de enfermedades por macroparásitos

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Reception date of the manuscript: dd/mm/aaaa
Acceptance date of the manuscript: dd/mm/aaaa
Publication date: dd/mm/aaaa

Abstract— In this work we present a general framework for the modeling of the transmission dynamics of macroparasites which do not reproduce within the host like *Ascaris lumbricoides*, *Trichuris trichiura*, *Necator americanus* y *Ancylostoma duodenale*. The basic models are derived from general probabilistic models for the parasite density-dependent mating probability. Here we considered the particular, and common case, of a negative binomial distribution for the number of parasites in hosts. We find the basic reproductive number and we show that the system exhibit a saddle-node bifurcation at some value of the basic reproduction number. We also found the equilibria and basic reproduction number of a model for the more general case of heteregeneous host populations.

Keywords—Basic reproductive number; Macroparasite; Mathematical modeling; Negative binomial distribution; Saddle-node bifurcation

Resumen— En este trabajo presentamos un marco general para el modelado de la dinámica de transmisión de macroparásitos que no se reproducen dentro del hospedador como *Ascaris lumbricoides*, *Trichuris trichiura*, *Necator americanus* y *Ancylostoma duodenal*. Los modelos básicos se derivan de modelos probabilísticos generales para la probabilidad de apareamiento denso-dependiente del parásito. Aquí consideramos el caso particular y común de una distribución binomial negativa para el número de parásitos en hospedadores. Encontramos el número reproductivo básico y mostramos que el sistema presenta una bifurcación nodo silla en algún valor del número reproductivo básico. También encontramos los equilibrios y el número básico de reproducción de un modelo para el caso más general de poblaciones heterogéneas de hospedadores.

Palabras clave—Bifurcación nodo silla; Distribución binomial negativa; Macroparásito; Modelo matemático; Número reproductivo básico

Introduction

Mathematical models play an important role in understanding the transmission and impact of macroparasite diseases control measures (Anderson and May, 1992; Anderson et al., 2014; Truscott et al., 2016).

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 (Leyton, 1968; Tallis and Leyton, 1966, 1969).

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 (Macdonald et al., 1965).

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 (Anderson and May, 1982, 1992).

In this article we develop an analytical framework to describe the transmission dynamics of most macroparasite infections. We first describe the dynamics of infection transmission by macroparasites. We then present two deterministic models for these transmission dynamics, the first for a homogeneous host community and the second for a heterogeneous host community.

In both models, reproductive characteristics of the parasite are considered, such as egg production and mating probabi-

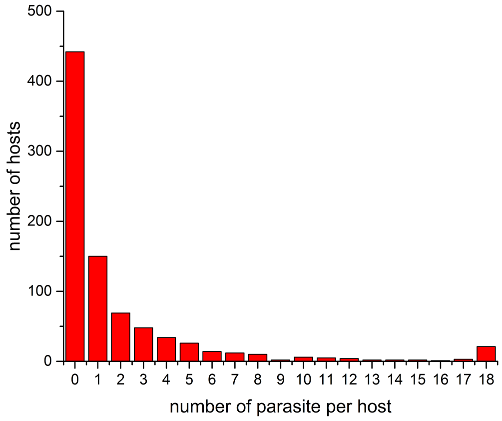

Figure 1: Distribution of *Ascaris lumbricoides* parasite numbers per host in a study in rural populations in Korea (Seo et al., 1979). Most hosts are uninfected or infected with a low burden of parasites while few are infected by large numbers of parasites.

lity, both modeled by the density-dependent fecundity of the parasite and the distribution of parasites per host, which we assume to be negative binomial.

For both models we present the calculations of the equilibrium values and the basic reproduction number R_0 defined for the case of macroparasites as the average number of new parasite offspring caused by a typical parasite, from one generation to the next. Finally for the homogeneous model we show that it has a saddle-node bifurcation.

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GENERAL FRAMEWORK

Microparasite diseases are usually modeled using compartmental models. After infection, microparasite population may rapidly grow into the host. This intra-host parasite dynamics determines the level of infectiousness of the individual. In a simple compartmental model like the SIR-model all the susceptible individuals are grouped in one class of size S, all the infected and infectious indviduals in a class of size I and all the recovered individuals in a class of size R. Many refinements are possible, but the evolution of the parasite population within the host it is not considered or very simplified (for models including intra-host population dynamics see for example Gandolfi et al. (2015)). The most common refinement consists in dividing infected individuals in two classes, exposed (those infected but not infectious yet) and infectious which leads to the well known $SEIR$ type models.

For most macroparasites the situation is completely different as these type of parasites do not reproduce within the host. Most infected individuals have few macroparasites with a non-bell shaped distribution (see Figure 1) where few individuals concentrate most of the parasites in the host population (Seo et al., 1979; Lopez and Aparicio, 2022b). Negative binomial distributions usually provide a good description of the data. On the other hand, there is no host-to-host transmission of macroparasites as life cycle completes in the environment (from where host get infected).

Therefore the number of infected hosts it is not a representative variable of the parasite burden. Simple models for macroparasites consider the evolution of the mean burden of parasite within the population as well as the environmental parasite reservoir (which is composed by eggs or larvae). From the mean burden, the total parasite population is easily estimated.

A BASIC MODEL

Model structure

The model presented in this paper is based on a model developed by Anderson and May (Anderson and May, 1992, 1985). The conceptual framework of parasite transmission dynamics is conceptualized as a population of mature parasites within human hosts and a population of infective stages (eggs or larvae) found in the environment (reservoir). Hosts can become infected by contact with the infective stages and can contaminate the environment with infective stages.

In a simple model for transmission dynamics of macroparasites in a population (where host demography is ignored) of size N of hosts the dynamic variables are the mean parasite burden of the population, m, and the infective stages in the environment formed by eggs or larvae, ℓ.

In the following we will sketch the procedure to find parasite-related parameters from a statistical-probabilistic model for the parasite population.

The environmental parasite reservoir, composed by eggs or larvae, increases due to the contribution of adult parasites within the hosts. As most host harbor only few parasites, only hosts with at least one female and one male parasites will contribute with fertilized eggs to the reservoir. We will consider that the random variable W, the number of parasites in a host follow a negative binomial distribution. Therefore, the probability of observing n parasites in a host is

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

where Γ is the gamma function, m is the mean value (the mean population parasite burden) and k the shape parameter, where the variance increases with the reciprocal of k as $\sigma^2 = m+m^2/k$. The term $\frac{k}{m+k}$ is the probability of success and $\frac{m}{m+k}$ is the probability of failure.

Mean egg production depends of the number of parasites within the host, it is a density-dependent process. A simple model for the mean female fecundity of a female parasite in competition with $n-1$ parasites is given by

$$\lambda(n)=\lambda_0 z^{n-1}, \tag{2}$$

where λ_0 is the rate of egg production per female independent of parasite density in host and $z=e^{-\gamma}$ with γ a parameter quantifying the intensity of the competition. A study of the *Ascaris lumbricoides* fecundity is presented in Hall and Holland (2000).

Using the parasite host distribution (1) we may compute the mean egg production per host as (Lopez and Aparicio, 2022a) $\lambda_0 \alpha m \psi(m,k,z)$ where α is the fraction of female parasites in a host and ψ is given by

$$\psi(m,k,z)=\left[1+(1-z)\frac{m}{k}\right]^{-(k+1)}. \tag{3}$$

This is called the average effective contribution per woman parasite to the parasite reservoir and can be obtained as in Churcher et al. (2006); Lopez and Aparicio (2022a).

However, only hosts with at least one female parasite and one male parasite will effectively contribute to the parasite reservoir by the production of fertilized eggs or infective eggs. Therefore, the mean fertilized egg production per host is

$$\lambda_0 \alpha m \psi(m,k,z)\phi(m,k,z), \tag{4}$$

where $\phi(m,k,z)$ is the mating probability for the negative binomial distribution computed in Lopez and Aparicio (2022a)

$$\phi(m,k,z) = 1 - \left[\frac{1+(1-\alpha z)\dfrac{m}{k}}{1+(1-z)\dfrac{m}{k}}\right]^{-(k+1)}. \tag{5}$$

Therefore, the mean fertilized egg contribution to the environmental reservoir per host and per unit of time is $\rho\lambda_0\alpha m\psi(m,k,z)\phi(m,k,z)$ where ρ is the host's own contribution rate and the total contribution of eggs to the reservoir per unit of time of a host population N is $\rho\lambda_0\alpha m\psi(m,k,z)\phi(m,k,z)N$.

The population of eggs or larvae in the environment (ℓ) also decreases due to egg/larval mortality (μ_ℓ) or due to host infection at the rate $\beta\ell$ per host. Therefore, the dynamics of the reservoir is given by

$$\frac{d\ell}{dt} = \rho\lambda_0\alpha m\psi(m,k,z)\phi(m,k,z)N - \mu_\ell\ell - \beta N\ell. \tag{6}$$

Finally, the dynamics for the mean parasite burden m is obtained as follow. Parasites are taken from the environment at a rate $\beta N\ell$ and therefore, the mean parasite burden increases at a rate $\beta N\ell/N = \beta\ell$. Parasites within the host die at a rate μ_p and hosts at a rate μ_h (killing all their parasites). Thus, the dynamics of m is given by

$$\frac{dm}{dt} = \beta\ell - (\mu_h+\mu_p)m. \tag{7}$$

Therefore, a basic model of the transmission dynamics of macroparasite diseases in a homogenous host population is given by the following the system of nonlinear ordinary differential equations

$$\begin{aligned}\frac{dm}{dt} &= \beta\ell - (\mu_h+\mu_p)m,\\ \frac{d\ell}{dt} &= \rho\lambda_0\alpha m\psi(m,k,z)\phi(m,k,z)N - \mu_\ell\ell - \beta N\ell.\end{aligned} \tag{8}$$

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Equilibria and basic reproduction number

In this section, we show the equilibrium values of the dynamical system (8), defined as the solutions of a dynamical system where the state variables do not change with time. We also obtain the basic reproduction number R_0 defined as the average number of female offspring produced per female adult worm, that survive to reproductive maturity in the absence of density-dependent constraints on parasite population growth (Anderson and May, 1992).

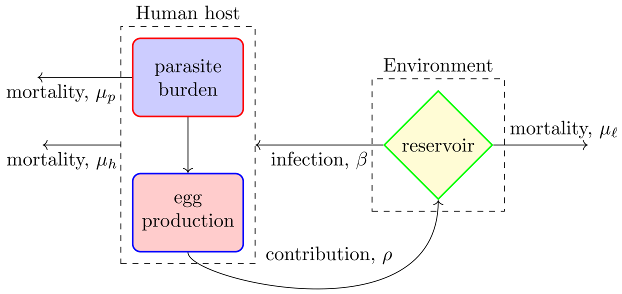

Figure 2: Conceptual framework of parasite transmission dynamics.

From the equation (6) we obtain that in the equilibrium

$$\ell^* = \frac{\lambda_0\alpha}{(\mu_\ell+\beta N)}\rho N m\psi(m)\phi(m), \tag{9}$$

and substituting (9) in equation (7) we obtain the following equation for the dynamics of m

$$\frac{dm}{dt} = (\mu_h+\mu_p)\left[R_0\psi(m)\phi(m)-1\right]m, \tag{10}$$

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

$$R_0 = \frac{\lambda_0\alpha\rho\beta N}{(\mu_\ell+\beta N)(\mu_h+\mu_p)}, \tag{11}$$

where for a large N value $R_0 \approx \frac{\lambda_0\alpha\rho}{(\mu_h+\mu_p)}$.

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Therefore from the equation (10) we can obtain the equilibrium condition for the mean parasite burden

$$\psi(m^*,k,z)\phi(m^*,k,z) = 1/R_0. \tag{12}$$

This equation present two equilibrium solutions for the mean parasite burden.

As shown in the next section, by a bifurcation analysis we obtain that the dynamic system (8) present a saddle-node bifurcation. The bifurcation occurs at the point (m^b, R_0^b) where

$$\begin{aligned} m^b &= \frac{k\left(\frac{1-\alpha z}{1-z}\right)^{\frac{1}{k+2}} - k}{(z-1)\left(\frac{1-\alpha z}{1-z}\right)^{\frac{1}{k+2}} + (1-\alpha z)},\\ R_0^b &= \left[\psi(m^b;k,z)\phi(m^b;k,z)\right]^{-1}. \end{aligned} \tag{13}$$

Therefore, for $R_0 > R_0^b$ there are three equilibria in the dynamic system (8) (see Figure 3),

- An equilibrium is the ***disease-free equilibrium*** present at $m^* = 0$, which is the trivial solution of equation (10). This equilibrium is an attractor for all values of R_0.
- The other equilibrium is the ***endemic equilibrium***, which is one solution of equation (12). This equilibrium is an attractor for a range of values of $R_0 > R_0^b$.

- The last equilibrium is an ***unstable equilibrium*** and corresponds to the other solution of equation (12). This equilibrium is a repulsor in the phase plane, that is, a barrier where values of $m(t)$ above the unstable equilibrium are attracted towards the endemic equilibrium and values of $m(t)$ below the unstable equilibrium are attracted to the disease-free equilibrium.

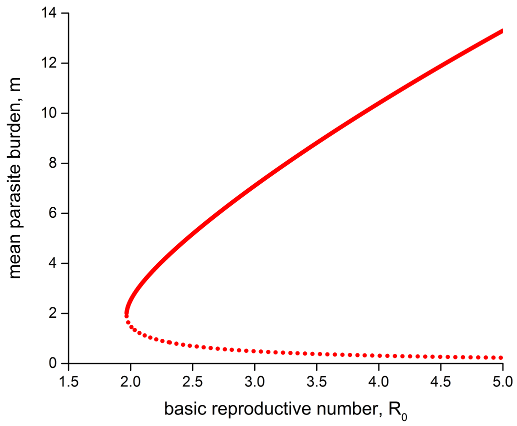

Figure 3: Saddle-node bifurcation generated by eq. (12), parameter values $\alpha = 0{,}57$, $k = 0{,}7$ and $z = 0{,}93$. The solid line and dotted line correspond to the stable and unstable branch, respectively.

Bifurcation analysis

Here, we show that the dynamic system (8) presents a saddle-node bifurcation. Assuming that the parasite reservoir is in equilibrium (9), the system reduces to one-dimensional system of the form

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

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

$$\begin{aligned} f(m^b, R_0^b) &= 0, \\ \frac{\partial f}{\partial m}(m^b, R_0^b) &= 0, \end{aligned} \tag{14}$$

where the first of these conditions is the equilibrium condition (12) of the dynamic system

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

and using the second condition of (14) we obtain the following equation for m^b

$$\frac{\partial}{m}\psi(m^b; k, z)\phi(m^b; k, z) = 0, \tag{15}$$

The value of m^b corresponding to this last condition is

$$m^b = \frac{k\left(\frac{1-\alpha z}{1-z}\right)^{\frac{1}{k+2}} - k}{-(1-z)\left(\frac{1-\alpha z}{1-z}\right)^{\frac{1}{k+2}} + (1 - \alpha z)}, \tag{16}$$

and its corresponding basic reproductive number is

$$R_0^b = \left[\psi(m^b; z, k)\phi(m^b; z, k)\right]^{-1}, \tag{17}$$

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

$$\begin{aligned} \frac{\partial f}{\partial R_0}(m^b, R_0^b) &\neq 0 \\ \frac{\partial^2 f}{\partial m^2}(m^b, R_0^b) &\neq 0 \end{aligned} \tag{18}$$

By a Taylor series expansion of the function f in a neighborhood of (m^b, R_0^b), the equation (10) is given by

$$\begin{aligned} \frac{dm}{dt} = f(m^b, R_0^b) &+ (m - m^b)\frac{\partial f}{\partial m}\Big|_{(m^b, R_0^b)} + (R_0 - R_0^b)\frac{\partial f}{\partial R_0}\Big|_{(m^b, R_0^b)} \\ &+ \frac{1}{2}(m - m^b)^2 \frac{\partial^2 f}{\partial m^2}\Big|_{(m^b, R_0^b)} + \cdots \end{aligned} \tag{19}$$

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

$$\frac{dm}{dt} = A(R_0 - R_0^b) + B(m - m^b)^2, \tag{20}$$

where the values A and B are

$$A = (\mu_h + \mu_p)\frac{m^b}{R_0^b}, \qquad B = (\mu_h + \mu_p)R_0^b m^b \frac{\partial^2 F}{\partial m^2}(m^b), \tag{21}$$

with $F(m) = \psi(m, z, k)\phi(m, z, k)$, which is the normal form of a saddle-node bifurcation.

Sensitivity analysis of the model parameters

To develop better control measures for macroparasitic diseases, it is necessary to know the relative importance of the different factors responsible for transmission.

The transmission of macroparasitic diseases is related to the value of R_0. To predict which parameters have a higher impact on R_0, we must perform a sensitivity analysis on R_0.

The elasticity index o normalized sensitivity index measures the relative change of R_0 with respect to a parameter x, denoted by $\Gamma_x^{R_0}$, and defined as (see Van den Driessche (2017))

$$\Gamma_x^{R_0} = \frac{\partial R_0}{\partial x}\frac{x}{R_0}, \tag{22}$$

The sign of $\Gamma_x^{R_0}$ tells whether R_0 correlates positively or negatively with the parameter x; whereas its magnitude determines the relative importance of the parameter.

For this model, the calculation of the elasticity indices are given by

$$\begin{aligned} \Gamma_{\lambda_0}^{R_0} &= \Gamma_{\alpha}^{R_0} = \Gamma_{\rho}^{R_0} = 1, \\ \Gamma_{\mu_h}^{R_0} &= -\frac{\mu_h}{\mu_h + \mu_p}, \\ \Gamma_{\mu_p}^{R_0} &= -\frac{\mu_p}{\mu_h + \mu_p}, \end{aligned} \tag{23}$$

if $\frac{1}{\mu_h} \gg \frac{1}{\mu_p}$, then $\Gamma_{\mu_p}^{R_0} \approx -1$ and $\Gamma_{\mu_h}^{R_0} \approx 0$. In Figure 4 illustrated the sensitivity indices of R_0 which were obtained and evaluated using parameter values $\mu_h = \frac{1}{70}$ and $\mu_p = 1$.

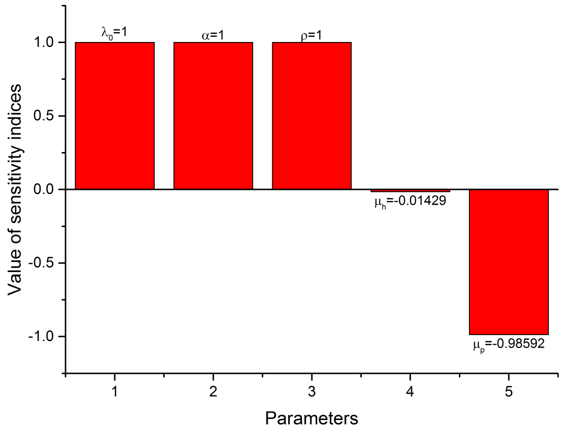

Figure 4: Sensitivity analysis for R_0 with respect to each model parameter.

Clearly the most sensitive parameters for R_0 are λ_0, α, ρ and μ_p. However, λ_0 and α correspond to parameters related to the life-cycle of the parasite which are quite difficult to modify, so a control measure for macroparasitic diseases should target to the reduction of ρ and/or the increase of μ_p.

Therefore, we can conclude from this analysis that the reduction of R_0 is possible by reducing the egg contribution from the hosts to the reservoir, for example, by building latrines in the host community or by increasing parasite mortality, for example, through the application of periodic and specific antiparasitic treatments.

A heterogeneous model

In this section, we consider the most general and realistic case of a host population. Unlike the homogeneous model presented in the previous section, here we present a model that accounts for the heterogeneity of the host population.

For this model, we assume that a host population, H, is divided into subpopulations or groups, H_i, that present different characteristics, which provide their hosts with distinct risks of infection (for example, by age groups, risk groups, environmental conditions, access to sanitation and hygiene, etc. Anderson and May (1992); Anderson et al. (2014); Brooker et al. (2006); Freeman et al. (2015); Truscott et al. (2014)).

The dynamics of parasitic infection for the case of a heterogeneous population is described as follows

$$\begin{aligned}\frac{dm_i}{dt} &= \beta_i \ell - (\mu_h + \mu_p) m_i \\ \frac{d\ell}{dt} &= \lambda_0 \alpha \sum_i N_i \rho_i m_i F(m_i) - (\mu_\ell + \sum_i \beta_i N_i)\ell,\end{aligned} \tag{24}$$

where $i = 1, \ldots, n$ with n the number of groups in H. The other parameters are detailed as follows and correspond to each group H_i

- m_i is the mean parasite burden,
- β_i and ρ_i are the rate of contact (or exposure) and the rate contribution of a host to the reservoir ℓ, respectively,
- N_i is the number of host,
- F is a product of two function: the mean effective contribution per female parasite to the reservoir, ψ (see eq (3)), and the mating probability, ϕ (see eq (5)).

the rest of the parameters are defined as in the previous section .

Equilibria and basic reproduction number

From the system (24) we obtain that in equilibrium

$$\ell^* = \frac{\lambda_0 \alpha}{(\mu_\ell + \sum_i N_i \beta_i)} \sum_i \rho_i N_i m_i F(m_i) \tag{25}$$

and substituting this in the rest of the equations of the initial system (24), we obtain the following equation for the dynamics of the mean parasite burden, m_i, of the host group H_i

$$\frac{dm_i}{dt} = \beta_i \frac{\lambda_0 \alpha}{(\mu_\ell + \sum_j N_j \beta_j)} \sum_j \rho_j N_j m_j F(m_j) - (\mu_h + \mu_p) m_i \tag{26}$$

where $j = 1, \ldots, n$.

The mean parasite burden m of the host population is given by

$$m = \sum_i \pi_i m_i \tag{27}$$

where π_i is the portion of the population H corresponding to the subpopulation H_i. The dynamic of mean parasite burden is described by

$$\frac{dm}{dt} = \left(\sum_i N_i \beta_i\right) \frac{\lambda_0 \alpha}{(\mu_\ell + \sum_j N_j \beta_j)} \sum_j \rho_j \pi_j m_j F(m_j) - (\mu_h + \mu_p) m \tag{28}$$

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

$$\sum_i \pi_i \frac{\lambda_0 \alpha \rho_i}{(\mu_\ell + \sum_j N_j \beta_j)(\mu_h + \mu_p)} \left(\sum_j N_j \beta_j\right) \times F(m_i^*) m_i^* - m^* = 0 \tag{29}$$

where m_i^* is the equilibrium mean parasite burden correspond to each group H_i. An equilibrium condition for m_i^* is given by

$$F(m_i^*) = \frac{1}{R_0^i}, \tag{30}$$

where we define the basic reproductive number of each group H_i by

$$R_0^i = \frac{\lambda_0 \alpha \rho_i}{(\mu_\ell + \sum_j N_j \beta_j)(\mu_h + \mu_p)} \left(\sum_j N_j \beta_j\right), \tag{31}$$

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. Note what for a large N value the reproductive number for each H_i is given by

$$R_0^i \approx \frac{\lambda_0 \alpha \rho_i}{(\mu_h + \mu_p)}, \tag{32}$$

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Also for this equilibrium situation, we obtain from equation (26), that the equilibrium mean parasite burden of each group H_i is given by

$$m_i^* = \frac{\beta_i \sum_j R_0^j \pi_j m_j^* F(m_j^*)}{\sum_j \pi_j \beta_j}. \qquad (33)$$

Note that this is not an explicit expression for the equilibrium m_i^*. Therefore, the equilibrium value can only be solved numerically.

The general basic reproductive number R_0 for the total population is given by

$$R_0 = \frac{\lambda_0 \alpha}{(\mu_\ell + \sum_j N_j \beta_j)(\mu_h + \mu_p)} \sum_j N_j \rho_j \beta_j, \qquad (34)$$

where we assume the absence the effects of density-dependence and the mating probability (Anderson and May, 1992), that is, we assume in the system (24) the function F equal to unity. A relationship between R_0 and R_0^i is given by

$$R_0 = \frac{\sum_i \pi_i \beta_i R_0^i}{\sum_i \pi_i \beta_i}, \qquad (35)$$

therefore we obtained that $\text{mín} R_0^i \leq R_0 \leq \text{máx} R_0^i$, then we can interpret to R_0 as an average value of the R_0^i.

Discussion and Conclusions

In this work, we developed deterministic mathematical models for the transmission dynamics of macroparasite infections.

We show how fundamental parameters related to production of fertilized parasites eggs are estimated from statistical models for the distribution of parasites within hosts.

We considered both homogeneous and heterogeneous host communities. The analyzed models show that the basic reproduction number R_0 strongly depends on the host egg contributions to the reservoir (which depend of the parameters ρ, α, and the parasite fecundity at low densities λ_0), and on the parasite mortality (μ_p). Therefore, to achieve a reduction in R_0 we must, for example, build latrines in the host community or implement regular and specific antiparasitic treatments.

For the homogeneous model we present a bifurcation analysis and show that this model exhibits a saddle-node bifurcation. The bifurcation parameter depends on the functions ψ and ϕ which in turn depend on the assumed distribution of parasites (see Lopez and Aparicio (2022a)).

More refined models may be developed from the simple models presented here which may be useful in the design and evaluation of different control strategies.

Acknowledgments

This work was partially supported by grant CIUNSA 2018-2467. JPA is a member of the CONICET. GML is a doctoral fellow of CONICET.

References

[1] Anderson, R. and May, R. (1982). "Population dynamics of human helminth infections: control by chemotherapy". *Nature*, 297(5867):557–563.

[2] Anderson, R. and May, R. (1985). "Helminth infections of humans: mathematical models, population dynamics, and control". *Advances in parasitology*, 24:1–101.

[3] Anderson, R. and May, R. (1992). *Infectious diseases of humans: dynamics and control*. Oxford university press.

[4] Anderson, R., Truscott, J., and Hollingsworth, T. (2014). "The coverage and frequency of mass drug administration required to eliminate persistent transmission of soil-transmitted helminths". *Philosophical Transactions of the Royal Society B: Biological Sciences*, 369(1645):20130435.

[5] Brooker, S., Alexander, N., Geiger, S., Moyeed, R. A., Stander, J., Fleming, F., Hotez, P. J., Correa-Oliveira, R., and Bethony, J. (2006). "Contrasting patterns in the small-scale heterogeneity of human helminth infections in urban and rural environments in brazil". *International journal for parasitology*, 36(10-11):1143–1151.

[6] Churcher, T. S., Filipe, J. A., and Basáñez, M. G. (2006). "Density dependence and the control of helminth parasites". *Journal of animal ecology*, 75(6):1313–1320.

[7] Freeman, M., Chard, A., Nikolay, B., Garn, J., Okoyo, C., Kihara, J., Njenga, S., Pullan, R., Brooker, S., and Mwandawiro, C. (2015). "Associations between school-and household-level water, sanitation and hygiene conditions and soil-transmitted helminth infection among kenyan school children". *Parasites & vectors*, 8(1):1–13.

[8] Gandolfi, A., Pugliese, A., and Sinisgalli, C. (2015). "Epidemic dynamics and host immune response: a nested approach". *Journal of mathematical biology*, 70(3):399–435.

[9] Hall, A. and Holland, C. (2000). "Geographical variation in ascaris lumbricoides fecundity and its implications for helminth control". *Parasitology Today*, 16(12):540–544.

[10] Leyton, M. (1968). "Stochastic models in populations of helminthic parasites in the definitive host, ii: sexual mating functions". *Mathematical Biosciences*, 3:413–419.

[11] Lopez, G. and Aparicio, J. (2022a). "General model of sex distribution, mating probability and egg production for macroparasites with polygamous mating system". *arXiv preprint arXiv:2202.11552*.

[12] Lopez, G. and Aparicio, J. (2022b). "Simple models for macroparasite distributions in hosts". *arXiv preprint arXiv:2202.11282*.

[13] Macdonald, G. et al. (1965). "The dynamics of helminth infections, with special reference to schistosomes." *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 59(5):489–506.

[14] Seo, B. S., Cho, S. Y., and Chai, J. Y. (1979). "Frequency distribution of ascaris lumbricoides in rural koreans with special reference on the effect of changing endemicity". *Korean J Parasitol*, 17(2):105–113.

[15] Tallis, G. and Leyton, M. (1966). "A stochastic approach to the study of parasite populations". *Journal of Theoretical Biology*, 13:251–260.

[16] Tallis, G. and Leyton, M. (1969). "Stochastic models of populations of helminthic parasites in the definitive host. i". *Mathematical Biosciences*, 4(1-2):39–48.

[17] Truscott, J., Hollingsworth, T. D., and Anderson, R. (2014). "Modeling the interruption of the transmission of soil-transmitted helminths by repeated mass chemotherapy of school-age children". *PLoS neglected tropical diseases*, 8(12):e3323.

[18] Truscott, J., Turner, H., Farrell, S., and Anderson, R. (2016). "Soil-transmitted helminths: mathematical models of transmission, the impact of mass drug administration and transmission elimination criteria". *Advances in parasitology*, 94:133–198.

[19] Van den Driessche, P. (2017). "Reproduction numbers of infectious disease models". *Infectious Disease Modelling*, 2(3):288–303.