A Model to Evaluate the Effects of Resistance and Tolerance on Performance

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Introduction

The fate of a pathogen within a domesticated animal population depends upon the natural defenses of the hosts and the management strategies of the breeder. Hosts may evolve resistant and tolerant defenses that reduce the deleterious effects of the parasite on performances. When these defenses are heritable, breeders can select animals with the highest levels of resistance, tolerance or both. The impact of the chosen selection strategies on the performances and the spread of the disease are different. Indeed, resistant hosts act directly on the parasite to reduce the success of infection or to increase the rate of clearance while tolerant ones act on the performance by reducing the detrimental effects of the parasite. Resistance and tolerance generate also fitness costs that arise from the diversion of limiting resources away from present and future performances. It is therefore important for a breeder to determine which strategy will maximize performance.

Here, we proposed a stochastic model that describes the parasite growth within each host and the consequences of this growth on the performances of the host for different degrees of resistance and tolerance.

Material and methods

The model. The model is for the spread of an SIS epidemic in a closed population of N individuals (Hethcote, 1995). The model is said to be of SIS type, because the susceptible hosts become infectious and then are susceptible again upon recovery from the infection. The newly infected individuals are immediately able to infect other individuals (no latent period). Once the individual is infected, the parasite population increases and the host's immune system is activated in an attempt to clear the infection. The performances of infected hosts decrease proportionally to the parasite load and to the investments put by the animal in the mechanisms of defense against the parasites.

Let C^i_t denotes the number of parasites in the i^{th} host at time t. Then in the stochastic version of the SIS model (Ross,1995), $\{C^i_t;\ t \geq 0\}$ is a continuous time Markov chain with three transition probabilities, each expressed per unit of time. The first probability is the probability for a susceptible to become infected by C_{min} parasites, i.e, the minimum number of parasites necessary to start the multiplication (as opposed to colonization). It is assumed directly proportional to the frequency (not the density) of infectious hosts with which it has contacts (Begon et al., 2002):

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$$\Pr(C^i_{t+1} = C_{min} | C^i_t = 0) = (\beta^k x^k y^k)/(x^k + y^k)\,\Delta t + o(\Delta t)$$

where β^k is the per-capita rate of infection for a susceptible in contact with y^k infectious individuals sharing the k^{th} degree of additive genetic relationship per unit of time.

It can be shown (Detilleux, 2005) that $\beta^k = \beta + a^k h^2 (1-\beta)$ where a^k is the degree of additive genetic relationship between animals in contact, h^2 is the heritability of the resistance to infection, and β denotes the 'global' transmission probability. This formulation is comparable to what is observed in SIS household epidemic models in which any infectious individual has two types of contact: the 'global contact' when the contacted host is selected randomly from the entire population and the additional 'local contact' when the contacted host belongs to the same household (Ball, 1999). Households are considered here as (overlapping) groups of related individuals containing x^k susceptible and y^k infectious individuals.

The second probability is the probability a parasite gives birth to m new offspring:

$$\Pr(C^i_{t+1} = c + m | C^i_t = c) = C^i_t \{\gamma (1-(C^i_t/K)\}\,\Delta t + o(\Delta t),$$

where γ is the per-capita growth rate. The number of parasites increases following a logistic or S-curve growth. At start, the growth is approximately exponential but it slows down as it reaches a maximum (K) at which it stops.

The last probability is the probability for a parasite to be killed:

$$\Pr(C^i_{t+1} = C_{min} | C^i_t = 0) = -\rho_i \mu\,\Delta t + o(\Delta t).$$

It follows from the dynamics observed in experimental studies between the numbers of bacteria and inflammatory cells (Detilleux, 2004; Li et al., 2002). The parameter μ represents the maximum number of pathogens killed per unit of time and ρ^i is a scaling parameter representing the relative level of resistance of the i^{th} host with respect to μ: If $\rho^i = 0$, the i^{th} host is not resistant at all and cannot recover. The unity is the highest value for ρ.

Once C^i_t is calculated, its effects on the performance of an infected host are modeled as:

$$P^i_t = P^i_{t=0} - C^i_t \omega (1 - \lambda^i),$$

where P^i_t is the performance of the i^{th} host infected with C^i_t pathogens, ω is the highest amount of performance lost per pathogen (virulence). The parameter λ^i is a scaling parameter representing the relative value of tolerance. If $\lambda^i = 1$, the i^{th} host is completely tolerant and produces at a level identical to the one without infection. If $\lambda^i = 0$, the host is not tolerant.

Hosts invest some of their energy to resist or tolerate any type of pathogen and these costs are assumed proportional to the investment in both types of defense. They are combined in an additive way (Restif and Koella, 2004):

$$P^i_{t=0} = P^{Max} (1 - \rho^i c^i_\rho - \lambda^i c^i_\lambda),$$

where P^{Max} is the maximal level of performance reached when there are no 'investment' in resistance and tolerance. The parameter c^i_ρ is the relative costs of resistance and c^i_λ is the relative cost of tolerance and is computed as $\alpha\, c^i_\lambda$. Values for both costs are limited so the factor within bracket is positive, $\rho^i c^i_\rho - \lambda^i c^i_\lambda \leq 1$, which implies some links exist between resistance and tolerance: $0 \leq c^i_\rho \leq 1/(1+\alpha)$. The maximum loss was set such that $P^i_{t=0} = 0$ when $C^i_{t=0} = K$ and $\lambda = 0$.

Statistical analyses. The Markov chain was simulated using the Gillespie algorithm (1977), essentially using exponential waiting times between events, where events are transitions between states.

Results and discussion

Within-host parasitic growth and individual performances are shown in the figure, for a population consisting at start of 30 hosts among which 2 were infected and able to transmit the infection. The number of parasites was followed across time (C^i_t) for each individual (i = 1 to 30 and t = 1 to 300) and the performances of each host (P^i_t) were updated accordingly. The values used for the reference population are: $\beta = 0.08$; $\gamma = 0.5$; $K = 500$; $\omega = 0.2$; $\mu = 0.5$; $\alpha = 1$; $c_\rho = c_\lambda \sim U[0,½]$; and $\rho, \lambda \sim U[0,1]$. In this reference population, all animals are unrelated ($\beta^k = \beta$).

When ρ and λ are the highest, C^i_t (solid line) and P^i_t (broken line) do not change across time and their values varied according to the associated costs (c_ρ, c_λ). When ρ and λ are low, the parasitic population increased up to its maximum, the performance decreased accordingly, and the impact of c_ρ and c_λ is negligible. Between these extremes, one may observe a wide range of different situations, some of which may lead to similar performance levels. For example, when $\lambda = 0$, the loss in performance will be similar in at least 2 different situations, i.e., when $\rho = 0.5$ at almost no costs ($c_\rho = 0.01$) and when $\rho = 0.9$ with $c_\rho = 0.3$. By varying the values of the parameters (sensitivity analyses), the effect of different levels of resistance, tolerance or both can be quantified by comparing the results to the population of reference.

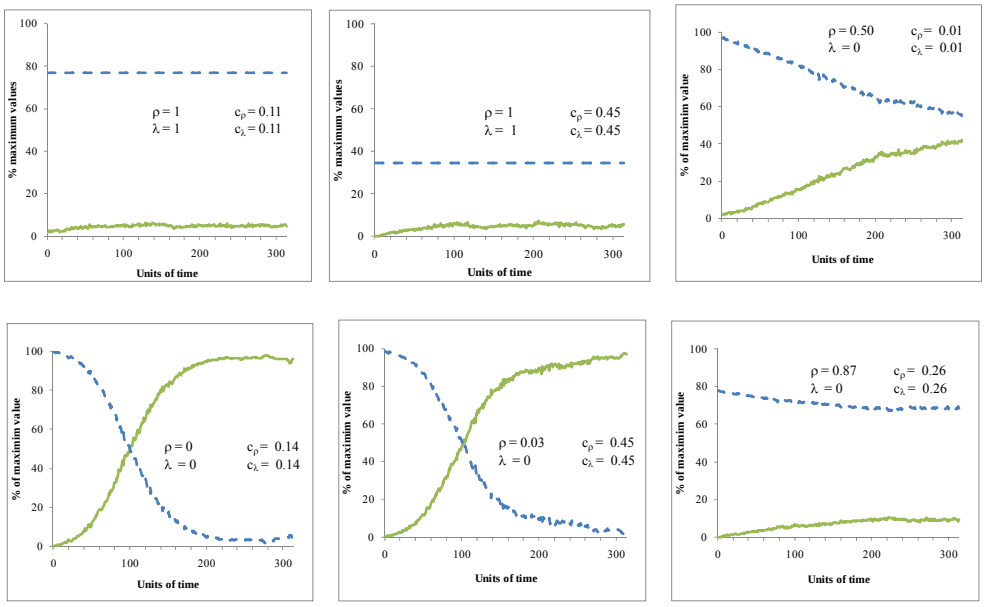

Figure 1: Number of parasites and performance per unit of time in individuals with different values for the model parameters.

Conclusion

These results show that the model could be useful to estimate the effects of varying degree of resistance, tolerance or both on the performance and degree of infection in hosts. Going at the population level, the model could also evaluate the effects on the spread of the infection.

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