Title

Effect of host populations on the intensity of ticks and the prevalence of tick-borne pathogens: how to interpret the results of deer exclosure experiments

Abstract

Deer are important hosts for feeding *Ixodes ricinus* ticks but they do not support transmission of many tick-borne pathogens, so acting as dead-end transmission hosts. Mathematical models show their role as tick amplifier, but also suggest that they dilute pathogen transmission, thus reducing infection prevalence. Empirical evidence for this is incongruous: experimental plots with deer removal show that the effect depends on the size of the exclosure. We present here simulations of a dynamical model that takes into account different tick stages, and several hosts that may move from and to deer exclosures; parameters were calibrated with respect to *Ixodes ricinus* ticks and tick-borne encephalitis (TBE) in Trentino (northern Italy). The results show that density of ticks feeding on rodents may be higher in small exclosures than outside, while a reduction is reached only with large exclosures. Similarly, TBE seroprevalence in rodents decreases in large exclosures, and may be slightly higher than outside in small exclosures. The density of infected questing nymphs inside a small exclosure can be much higher, in our numerical example more than twice, than outside, leading to the potential TBE infection risk hotspot.

1. Introduction

Tick-borne infections are caused by pathogens transmitted between hosts by ticks that become infected following a blood meal. Among the zoonotic tick-borne diseases, tick-borne encephalitis (TBE), Lyme disease, rickettsiosis, ehrlichiosis are emerging as international human health threats (Hudson *et al.*, 2002).

These infections are characterized by an intricate set of ecological and epidemiological relationships between pathogen, tick vector, vertebrate hosts, and humans, which largely determine their spatial distribution and temporal dynamics. Tick distribution is certainly influenced by meteorological factors, so that accurate up-to-date information about microclimate conditions have been correlated with tick population dynamics and its distribution (Randolph *et al.*, 1999). However, tick-borne foci of infection tend to occur at a fine scale determined in part by the spatial distribution and abundance of competent host species for tick-borne pathogen transmission in relation with non-competent host species (Van Buskirk and Ostfeld, 1995; Ostfeld and Keesing, 2000). As ticks can feed on many different animals and every species has a unique reservoir competence, or ability to carry and transmit the pathogen, the presence of different food sources might affect disease incidences. For Lyme disease in the US, where the most important reservoir is the white-footed mouse, it has been shown that the greater the relative abundance of non-mouse hosts, the lower the percentage of ticks infected with Borrelia (Ostfeld and Keesing, 2000); this phenomenon has been named "dilution effect", meaning that the presence of non-competent hosts, such as white-tailed deer, dilutes the transmission of tick-borne pathogens, decreasing their prevalence and subsequent disease risk to humans.

Several mathematical models have been developed (Hudson *et al.*,1995; O'Callaghan *et al.*,1998; Caraco *et al.*, 1998; Norman *et al.*, 1999; Rosà *et al.*, 2003; Rosà and Pugliese, 2007) that demonstrate theoretically the possibility of the dilution effect, and the conditions under which it may occur. However, its empirical validity and more generally the role of host densities on the prevalence of tick-borne infections is still debated (Perkins *et al.*, 2006).

A method to study the relevance of the "dilution effect" is to alter experimentally host densities. One of the simplest ways to modify host densities is to build exclosures that prevent the entrance of large mammals, such as deer. Therefore, several experiments of this type have been performed in different areas in the world (a subset of which is presented by Perkins *et al.*, 2006); however, the

exclosures have yielded equivocal outcomes, some resulting in tick reduction, others in tick amplification. Recently, Perkins *et al*. (2006) performed a meta-analysis of a sub-set of the published studies, showing that the results did indeed depend on the scale of the exclosures. Precisely, they found that small exclosures generally resulted in tick amplification, while large exclosures caused reductions in tick intensity, with the switch from tick amplification to reduction occurring when exclosures were larger than about 2.5 hectares. The general prediction from this meta-analysis was confirmed by some small experimental exclosures (less than 2.5 hectares in size), where rodent density, tick intensity and tick-borne encephalitis (TBE) prevalence were repeatedly measured inside and outside the exclosures. Perkins *et al.* (2006) found that the intensity of feeding nymphs and adult female ticks on rodents, but not larval intensity, were higher within deer exclosures than outside; moreover, rodents positive for TBE were found only where deer were absent.

The mechanisms that created tick amplification and a TBE hotspot at this small spatial scale remain elusive. Clearly, if deer are absent, ticks that are present on the exclosures will be more likely to feed on rodents, increasing tick load and the potential for infection transmission. On the other hand, the absence of deer, a very important host for feeding adult ticks, will reduce the long-term tick population, and this may decrease also the load on rodents. The balance between these two forces may in principle depend on rodent density and on the size of the exclosure compared to the typical scale of rodent movement; in fact, ticks may be carried on animals inside small exclosures, while this factor should be less important for large exclosures.

Here we explore the possible role of host density and exclosure size in increasing or decreasing tick load and infection prevalence through mathematical models. First, we consider a model for tick population dynamics, based on Rosà and Pugliese (2007), and investigate the predicted effect of host densities on tick population dynamics. Then, by extending the model with patches from which deer are assumed to be absent we study whether the model can help to explain the experimental

results of Perkins *et al*., (2006). Finally, we consider the dynamics of a tick-borne infection transmitted both systemically and non-systemically through co-feeding ticks (Randolph *et al*., 2002a), analysing the likely effect of deer exclosures.

2. Materials and methods

2.1 Mathematical models

2.1.1 Basic model for tick demography

To examine *Ixodes ricinus* dynamics we used a basic tick demography model following Rosà and Pugliese (2007). This model explores the dynamics of three tick stages: larvae (*L*), nymphs (*N*) and adults (*A*) by explicitly modelling questing (with subscript *Q*) and feeding (with subscript *F*) phases (see Appendix). It is assumed that ticks feed on two kind of hosts: small mammals (e.g. rodents), indicated with H_1, and medium to large-sized mammals (e.g. deer), indicated with H_2. For each tick stage (e.g., larvae) we then distinguish between those feeding on hosts 1 (L_{F_1}) and those feeding on hosts 2 (L_{F_2}).

The overall flux diagram is shown in Fig. 1. All transitions in the diagram are assumed to be density-independent, except that the production of larvae per feeding adult ticks is a decreasing function (following a fraction rule) of the number of ticks feeding on that type of hosts T_{F_i}; this assumption corresponds to the observation that past tick load stimulates the hosts' resistance to tick feeding, resulting in reduced egg production (Wikel, 1996). The rationale for this or other types of density-dependence is discussed at length in Rosà and Pugliese (2007), where a slightly different mathematical formulation is used.

Neglecting, for the sake of simplicity, seasonality in the tick-host interaction, and all developmental stages between one tick stage and the next, one arrives at the system of differential equations (1) reported in Appendix. A full list of parameters with their biological interpretation is given in Tab. 1.

2.1.2 Model for tick demography with deer exclosure

We add to the previous model a deer exclosure, assuming that deer (H_2) are present only outside the exclosure, while rodents (H_1) may move freely from and into the exclosure. We do not explicitly take account of space in the model, assuming that within each compartment (the exclosure and the rest of the habitat) interactions are homogeneous. Moreover, we assume that (except for the existence of a fence) the habitat is homogeneous, so that rodent density is the same inside and outside the exclosure.

The parameter ρ quantifies the movement of rodents from and into the exclosure and it is strictly related with the size of exclosure: for instance, where ρ is equal to 0.1, this means that 10% of the rodents initially present inside the exclosure move, in the time unit, outside of the exclosure. Clearly ρ depends on the ratio between the typical distance (in the time unit) of rodents' movement and the size of the exclosure: the higher is ρ, the smaller is the exclosure. Furthermore, to keep rodent density constant inside and outside the exclosure (neglecting stochastic fluctuations), we need to assume that, for each rodent that moves out of the exclosure, another one moves inside.

Rodents that move will carry the ticks feeding on them; hence, ticks feeding on these hosts (hosts 1) will move inside and outside the exclosure at the same rates as rodents. On the other hand, questing ticks will remain in the compartment in which they have developed, and there will be ticks feeding on hosts 2 only in the outside compartment (a sketch of the resulting flow chart can be inferred from Fig. 1, considering that the dashed lines connect two compartments, like the one presented).

In order to properly balance the equations, a further parameter is necessary, that of *scale*, the ratio of the areas inside and outside the exclosure. This parameter will affect the change of outside densities due to rodent emigration from the exclosure; when *scale* is set to zero (as we do in all simulations in this present paper, meaning that the exclosures are extremely small relative to the

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outside habitat), the movement of rodents from and to the exclosure does not affect rodent or tick density outside deer exclosure.

These assumptions lead to an easy modification of system (1). We need to consider the densities of all tick stages inside (indicated with superscript *IN*) and outside (with superscript *OUT*), and we obtain the system (2) reported in Appendix.

2.1.3 Model for tick-borne infections with deer exclosure

Finally, we consider the dynamics of a tick-borne infection. Tick-borne infections may have different competent hosts, and different infection pathways (Randolph *et al*., 1996; Randolph *et al*., 2002a). Here we consider the case where both systemic and non-systemic (through co-feeding ticks) transmission takes place only on rodents (competent hosts) while deer feed the tick population without amplifying the pathogen. These assumptions are adequate to describe the transmission of tick-borne encephalitis virus (Randolph *et al*., 2002a).

The system is built over the structure shown in Fig. 1, but distinguishing between susceptible, infected and infectious ticks; susceptible, infective and immune rodents. Ticks are born susceptible, may become infected via a blood meal from an infectious host, or a co-feeding tick; after developing to the next stage, the infected tick will become infectious. Analogously, rodents are born susceptible, may be infected by an infective tick feeding on them, and after a short infectious period (during which they suffer extra-mortality caused by the infection) they become permanently immune. The equations are reported in the system (3) (see Appendix) and analysed in Rosà and Pugliese (2007). Here, we consider a slightly more general case, letting adult ticks feed not only on deer but also on rodents; although the empirical evidence shows that rarely adult ticks feed on rodents, this possibility would allow the tick population to persist also within the exclosure where only rodents are present and was observed empirically by Perkins *et al*. (2006). On the other hand, the equations presented in Rosà and Pugliese (2007) include parameters for the probability for a tick [or a host] of getting infected after a blood meal on [by] an infective host [tick]; since here we are

mainly interested in qualitative effects on prevalence, and our model has already plenty of parameters, we fix these probabilities to 1, as in Foppa (2005).

The final modelling step is to introduce the exclusion of deer into the model (3), distinguishing, as in model (2), tick and rodent host stages between the inside (*IN*) and outside (*OUT*) of the deer exclosure (compartments). The resulting system, (not shown), consists of 32 differential equations and are available on the Web at http://www.science.unitn.it/~pugliese/.

2.2 Parameter values

Parameter values are calibrated to *Ixodes ricinus* tick and tick-borne encephalitis in Trentino (northern Italy) considering the following main host species: the most abundant rodent host, yellow-necked mouse (*Apodemus flavicollis*), and the main ungulate host, roe deer (*Capreolus capreolus*). The full list of parameters values are given in Tab. 1 where we measure time in days and densities in hectares^{-1} (ha^{-1}).

Carrying capacity for rodents is set to 15 mice per hectare while deer density is set to 10 per km^{2} (0.1 per hectare) according to density observed during field experiment (Rosà *et al*., in press). The mean lifespan of *A. flavicollis* is considered to be 270 days and number of offspring is assumed to be 6 per year, implying that host mortality d is 0.0037/day and host birth rate b, assuming 1:1 sex ratio, is 0.00821/day (Ferrari *et al*., 2007).

Concerning ticks' demographic parameters, adult females are thought to produce up to 5,000 eggs (data from the International scientific-Working Group on TBE: see http://www.tbe-info.com/tbe.aspx); hence, r_T is taken as 2,000, around half of that value to take into account the presence of male and female ticks. As for the parameter s_T of density-dependent, we set it to 0.25 in order to find equilibrium densities for feeding ticks comparable with what observed in the field (Rosà *et al*., in press). Tick mortalities are different for each life stage (Sonenshine, 1991; Randolph and Rogers, 1997) and are computed as 1/(average survival period of ticks on vegetation without finding a host) (see Tab. 1 for values). The detachment rate of ticks σ is given by 1/(feeding time)

and depends on tick stages (Sonenshine, 1991; data from the International scientific-Working Group on TBE: see http://www.tbe-info.com/tbe.aspx) (see Tab. 1 for values). The parameters m^L and m^N represent the probability of moulting success for larvae and nymphs after feeding. In reality, m^L and m^N may depend on the host species (Humair *et al.*, 1999), but, for the sake of simplicity, here we choose the same values for both hosts and we also choose the same value for larvae and nymphs setting $m^L=m^N=0.15$ (Humair *et al.*, 1999).

Empirical data on the densities of larvae and nymphal ticks questing and feeding on rodents were used to estimate encounter rates between rodents and ticks in different stages (Rosà, 2003; Rosà and Pugliese, 2007). On the other hand, no comparable measures existed to estimate the encounter rates of ticks with deer. An experiment with tracer animals (domesticated goats) was carried out obtaining the numerical values reported in Rosà and Pugliese (2007). Since ticks may be better adapted to their natural hosts, roe deer, than to domesticated goats, we generally used in this paper values of the tick-deer encounter rates higher than those estimated from the experiment; these are reported in Table 1, while in Fig. 2 we show the difference in results between the two sets of coefficients.

Probability of transmission of tick-borne encephalitis virus (TBEv) through co-feeding ticks λ are set to 0.5 in accordance with values measured in laboratory experiments by Labuda *et al.* (1993). Here, for the sake of simplicity, we assumed the same value for all possible co-feeding transmission among different tick stages: infected nymphs to larvae, infected to susceptible nymphs and infected adults to susceptible nymphs.

Finally TBEv-induced rodent mortality rate (α) and the recovery rate from infection (γ) are assumed lower than those reported in literature by Randolph *et al.* (1996); otherwise, we would obtain, using the tick-deer encounter rates of Tab. 1, a basic reproduction number (R_0) for TBEv smaller than 1. Indeed, other investigations show that TBEv seems to be close to the boundary of extinction using the reported parameter values of the infectious period (Foppa, 2005).

A very important parameter in the model with exclosures is ρ, the rate at which rodents exit the exclosures. As discussed above, this is inversely related to the exclosure size; this relation can be quantified using estimates for rodent home ranges. Home ranges for *A. flavicollis* have been determined by Schwartzenberger and Klingel (1995) to be around 1.5 ha for males and 0.38 ha for females, during breeding season. Recent observations in the study area (A. Stradiotto and F. Cagnacci, unpublished data) show a dramatic change in home range between years of high or low rodent density: calculated home ranges are close to the estimates by Schwartzenberger and Klingel (1995) in high-density years, but may be around 4.2 ha (for males) and 1.9 ha (for females) in low-density years. Taking an average of these measures, and assuming that a rodent explores half its home range in 1 day, we can roughly say that $\rho = 1$ corresponds to an exclosure of around 0.75-1 ha, and $\rho = 0.1$ corresponds to an exclosure of around 7.5-10 ha.

3. Results

3.1 Effect of hosts on tick densities

Fig. 2 shows how the equilibrium densities of questing larvae and nymphs, and of ticks feeding on rodents, change with densities of rodents (left panel) and of deer (right panel).

Increasing host densities makes it easier for a tick to find a host, and, because of the values of encounter rates, questing larvae are especially sensitive to rodent densities, while questing nymphs are more sensitive to deer densities.

This observation may help in understanding the shapes of the curves shown in Fig. 2. When hosts are scarce, finding a host is a limiting component for tick populations; hence, at low host densities, all curves increase with either host density.

On the other hand, in model (1) it is assumed that the ticks' reproductive success decreases with feeding tick density; hence, at high host densities, equilibrium tick density will reach a saturation level, and will only marginally be affected by further increases in host densities. This fact causes the

humped shape of the curves of questing larvae with respect to rodent densities, and of questing nymphs with respect to deer densities. The humped shape is a general feature under this type of density-dependence (see Rosà and Pugliese, 2007) and can be explained as follows: when rodent hosts are extremely abundant, the total number of ticks is almost independent of host densities, due to the saturation effect; hence, the rate at which new larvae are recruited is almost constant; the rate at which larvae feed on rodents (and thus leave the questing phase) is a strongly increasing function of the rodent density (H_1), since rodent hosts will be easier to find. An almost constant entrance rate and an always increasing exit rate makes the equilibrium level smaller and smaller, as clearly shown in Fig. 2. A similar argument holds for questing nymphs (and more weakly for larvae) and deer densities. On the other hand, equilibrium questing nymphs go on increasing with rodent densities (at least over the reasonable range shown in Fig. 2), because the entrance rate in the compartment (resulting from larvae feeding more and more on rodents) increases more than the exit rate (nymphs' feeding rates are less sensitive to rodent densities).

The shape, at high host densities, of the curves of feeding ticks can be easily explained by a competition effect: at an almost constant total level of ticks, increasing rodent densities will make more ticks feed on rodents (and less on deer), as seen in the left panel of Fig. 1; increasing deer densities will make less ticks feed on rodents (and more on deer), as seen in the right panel of Fig. 1.

3.2 Effect of deer exclosure on tick dynamics

We show (Fig. 3) the effect of the size of deer exclosure on tick populations taking the parameter *scale* equal to 0, i.e. assuming that the area outside the exclosure is much larger than the inside area; hence, densities outside do not depend on the presence of the exclosure or the exchange rate ρ. Other simulations (not shown) with a positive value of the parameter *scale* yield qualitatively similar results, although in that case outside tick densities will depend on the parameter ρ.

Precisely, Fig. 3 shows, on the *y*-axis, the densities of ticks (larvae, nymphs and adults) feeding on rodents (inside and outside deer exclosure) and on the *x*-axis, the value of the parameter ρ. We recall that ρ is the proportion of rodents exiting (in the time unit) the exclosure, hence it is an inverse measure of the size of exclosure: the higher the value of ρ the smaller the area within the deer exclosure.

In Fig. 3 we show results obtained with different values of encounters rates between deer and ticks (β_2): figures on the left panels of Fig. 3 (column *A*) are obtained with lower values of β_2 (those shown in Rosà and Pugliese, 2007); figures on the right panels of Fig. 3 (column *B*) are obtained with higher values of β_2 (Tab. 1). In both cases we show, for varying ρ, the densities of (from top to bottom) larvae, nymphs and adults feeding on rodents inside and outside the exclosure.

We see that, in both cases, densities of feeding larvae (top row of Fig. 3) are less inside the exclosure than outside, with the difference decreasing as the exclosure becomes smaller (ρ increases). On the other hand, only when the exclosure is large, densities of feeding adults are less inside than outside, but, for smaller exclosures (about $\rho > 0.1$) there are more adult ticks feeding on rodents inside than outside the exclosure (bottom row of Fig. 3), though the effect is rather weak especially for higher values of β_2 (right column). Finally the effect of exclosure size on the densities of feeding nymphs (middle row of Fig. 3) depends strongly on the values of β_2: when they are smaller (left column), densities are higher outside than inside, similarly to what happens for larvae; in the case of higher β_2 values (right column), densities inside the exclosure may be quite higher (about 25%) inside a small exclosure than outside, while a reduction is reached only with very large exclosures.

Fig. 3 shows only the densities obtained in the exclosures at equilibrium. It may be of interest studying the transient effects. Fig. 4 shows the temporal dynamics of feeding nymphs density on rodents after the introduction of deer exclosure. The right panel of Fig. 4 shows a simulation with a smaller exclosure ($\rho = 0.15$) while on the left panel the simulation of a larger exclosure is shown

(ρ=0.05). The removal of deer always results in a transient increase of feeding nymphs on rodents, but this effect lasts only for small exclosures (right panel of Fig. 3) while for larger exclosure (left panel of Fig. 3) a reduction in tick densities is observed after a short period of time (around one month in the simulation).

3.3 Effect of host densities on a tick-borne infection

Rosà and Pugliese (2007) discuss in detail the effects of host densities on the persistence of a tick-borme infection; they discussion the region (in the 2-dimensional plane of rodent and deer densities) in which the reproduction ratio R_0 is greater than 1, according to the type of transmission of the infection, and the modes of regulation of tick populations.

Here, for the only case of an infection transmitted systemically and by co-feeding on rodents (like TBEv) and the density-dependence law shown in equation (1), we show (Fig. 5) how the equilibrium prevalence depends on host densities. We can see that, as rodents densities increases above a minimum threshold density (around 13/ha with these parameter values), the prevalence of TBE in rodents and the density of infected questing nymphs (the stage more risky for transmission to humans) increase steadily. On the other hand, prevalence increases with deer density only when this is extremely low (less than $2/km^2$); further increases cause a reduction in infection prevalence, up to the point that, for deer density above an upper threshold (around $12/km^2$ with these parameter values), the infection cannot persist. This constitutes the "dilution" effect: an increase in density of species not competent for an infection dilutes the possibility of effective infection transmission, and makes its persistence more difficult.

It has to be noticed that the values obtained as boundaries for persistence (that are very close to the observed average values, used in our simulations, of 15 rodents/ha and 10 deer/km^2) depend strongly on the values used in our simulations (Tab. 1) that are somewhat different than most available estimates (see the Section on parameter estimates). The conditions allowing for the

persistence of TBEv are analysed more thoroughly by Randolph *et al.* (2002a), Foppa (2005), Rosà and Pugliese (2007).

Finally, it has to be remarked that it is theoretically possible that a dilution effect holds for rodents as well: if rodent density were extremely high, the tick/host ratio would decrease, making infection transmission less likely (Rosà and Pugliese, 2007). Indeed, if the axis displaying rodent density (on the left panel of Fig. 5) were prolonged up to densities around 500 rodents/ha, one would see a decrease in infection prevalence, and the curve would be similar to that of the right panel. However, it seems that (if parameter values are reasonable) this phenomenon occurs only for densities of rodents unrealistically high, so that it has no practical relevance.

3.4 Effect of deer exclosure on infection dynamics

Finally, we simulated the effect of exclosure size (varying ρ) on tick-borne encephalitis (TBE) infection, with particular attention to the density of infected questing nymphs inside and outside deer exclosures (left panel of Fig. 6) as it represents the most important variables in terms of human infection risk. The right panel of Fig. 6 shows the effect of exclosure size on TBE seroprevalence detected in rodents inside and outside deer exclosures. TBE seroprevalence in rodents decreases in large exclosures (about $\rho<0.1$), and is slightly higher than outside in small exclosures (right panel). Similarly, but with a much stronger effect, we see that the density of infected questing nymphs in small exclosures is much higher than outside. When the exclosure is very small ($\rho\approx1$, corresponding to around 0.75-1 ha), the density of infected questing nymphs inside is more than twice than outside, leading to the potential for TBE risk hotspot.

4. Discussion

Several observations (Ostfeld and Keesing, 2000) indicate that the density and the diversity of tick hosts are important determinants of the presence and the intensity of tick-borne infections. However, experiments in which host densities have been directly altered by setting plots from

which larger mammals (especially deer) were excluded have yielded equivocal results, with tick densities sometimes higher, sometimes lower, inside the experimental plots than outside. Perkins *et al.* (2006) have shown that a general rule could be inferred from the experimental plots: small exclosures tend to result in higher tick densities, large exclosures in lower tick densities. We show in the present paper that this rule is compatible with the predictions of the mathematical models used in recent years to describe tick-host interactions, when they are modified to allow for the presence of a deer exclosure.

It is certainly possible that deer removal results in a different type of habitat, for instance with a different vegetation cover, hence with different tick and host survival, and tick-host encounter rates. Thus, differences in tick densities could be explained on this basis. While it is very likely that deer removal will change several features of the habitat, these differences should not be highly influenced by the size of the exclosure plot. Thus, it seems difficult to explain the pattern shown by Perkins *et al.* (2006) on this basis.

Here, we have instead shown that, assuming that there is no habitat difference between inside and outside the plots, the basic mechanisms of tick-host interactions predict density effects in qualitative agreement with experimental data: large exclosures should result in lower densities of ticks in all stages, while small exclosures can result in relevant increases of tick densities, depending on parameter values and the tick stage (larva, nymph, questing, feeding) one looks at.

Thus, this simple mathematical models seems to be an agreement with the general pattern of the results of deer exclosures, although certainly more detailed information (on the habitat, host species, etc.) would be necessary to describe better each specific experiment. Thus, the analysis of the exclosure experiments seems to be in agreement with the assumption that tick populations are strongly influenced by host densities.

A particularly striking result of the simulations shown in this paper, is the potential increase in the densities of infected questing nymphs in small areas from which deer are excluded (left panel of Fig. 6). Although the model was built to describe experimental exclosures, it shows that there exists

potentially the risk that infective tick stages concentrate in small areas in which, for whatever reason, important not infection-competent hosts are absent.

It must certainly be recognized that several aspects of the model presented here are not particularly realistic. The models are based on differential equations with constant coefficients, thus disregarding seasonality and developmental delays, two features that are central in the dynamics of tick populations in temperate habitats (Randolph *et al*., 2002b; Rosà *et al*., in press). Models that take into account the existence of discrete growing seasons are considerably more complex to analyse (Ghosh and Pugliese, 2004), but their predictions should differ from those from differential equation models mainly in the dynamical properties and not in the equilibria, which have been the main subject of analysis here.

More central to the present analysis is the omission of space from the models. Although exclosures could be described adequately only by explicitly introducing space in the models, and random or directed animal movements, exclosures and the remaining habitat have been described here only as homogeneous compartments with a fixed exchange of rodents between them. This kind of modelling precludes the possibility of identifying boundary areas around the exclosure, which are affected by the experiments, and more generally spatial features of ticks' distribution. On the other hand, a spatial model would require better knowledge of animals' movement rules, and several more parameters to estimate. Moreover, differences between outside and inside areas would have to be inferred from a more complex structure of results. We believe that the present modelling of exclosures, though somewhat sketchy is quite adequate to the aim of qualitatively explaining the consequences of deer exclosures on tick densities.

and Maria-Gloria Basanez for organizing the very interesting workshop from which this special issue originates.

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Appendix

Model for tick dynamics without deer exclosure

$$\frac{dL_Q}{dt} = \frac{r^T}{1+s^T T_{F_1}}\sigma^A A_{F_1} + \frac{r^T}{1+s^T T_{F_2}}\sigma^A A_{F_2} - (\beta_1^L H_1 + \beta_2^L H_1)L_Q - d^L L_Q$$

$$\frac{dL_{F1}}{dt} = \beta_1^L H_1 L_Q - \sigma^L L_{F_1}$$

$$\frac{dL_{F2}}{dt} = \beta_2^L H_2 L_Q - \sigma^L L_{F_2}$$

$$\frac{dN_Q}{dt} = m^L \sigma_1^L (L_{F_1} + L_{F_2}) - (\beta_1^N H_1 + \beta_2^N H_1)N_Q - d^N N_Q$$

$$\frac{dN_{F1}}{dt} = \beta_1^N H_1 N_Q - \sigma^N N_{F_1} \tag{1}$$

$$\frac{dN_{F2}}{dt} = \beta_2^N H_2 N_Q - \sigma^N N_{F_2}$$

$$\frac{dA_Q}{dt} = m_1^N \sigma_1^N (N_{F_1} + N_{F_2}) - (\beta_1^A H_1 + \beta_2^A H_1)A_Q - d^A A_Q$$

$$\frac{dA_{F1}}{dt} = \beta_1^A H_1 A_Q - \sigma^A A_{F_1}$$

$$\frac{dA_{F2}}{dt} = \beta_2^A H_2 A_Q - \sigma^A A_{F_2}.$$

Model for tick dynamics with deer exclosure

$$\frac{dL_Q^{IN}}{dt} = \frac{r^T}{1 + s^T T_{F_1}^{IN}} \sigma^A A_{F_1}^{IN} - \beta_1^L H_1 L_Q^{IN} - d^L L_Q^{IN}$$

$$\frac{dL_{F_1}^{IN}}{dt} = \beta_1^L H_1 L_Q^{IN} + \rho L_{F_1}^{OUT} - \rho L_{F_1}^{IN} - \sigma^L L_{F_1}^{IN}$$

$$\frac{dL_Q^{OUT}}{dt} = \frac{r^T}{1 + s^T T_{F_1}^{OUT}} \sigma^A A_{F_1}^{OUT} + \frac{r^T}{1 + s^T T_{F_2}^{OUT}} \sigma^A A_{F_2}^{OUT} - (\beta_1^L H_1 + \beta_2^L H_2) L_Q^{OUT} - d^L L_Q^{OUT}$$

$$\frac{dL_{F_1}^{OUT}}{dt} = \beta_1^L H_1 L_Q^{OUT} + scale \cdot \rho L_{F_1}^{IN} - scale \cdot \rho L_{F_1}^{OUT} - \sigma_1^L L_{F_1}^{OUT}$$

$$\frac{dL_{F_2}^{OUT}}{dt} = \beta_2^L H_2 L_Q^{OUT} - \sigma^L L_{F_2}^{OUT}$$

$$\frac{dN_Q^{IN}}{dt} = m^L \sigma^N L_{F_1}^{IN} - \beta_1^N H_1 N_Q^{IN} - d^N N_Q^{IN}$$

$$\frac{dN_{F_1}^{IN}}{dt} = \beta_1^N H_1 N_Q^{IN} + \rho N_{F_1}^{OUT} - \rho N_{F_1}^{IN} - \sigma^N N_{F_1}^{IN}$$

$$\frac{dN_Q^{OUT}}{dt} = m^L \sigma^L (L_{F_1}^{OUT} + L_{F_2}^{OUT}) - (\beta_1^N H_1 + \beta_2^N H_2) N_Q^{OUT} - d^N N_Q^{OUT}$$ (2)

$$\frac{dN_{F_1}^{OUT}}{dt} = \beta_1^N H_1 N_Q^{OUT} + scale \cdot \rho N_{F_1}^{IN} - scale \cdot \rho N_{F_1}^{OUT} - \sigma^N N_{F_1}^{OUT}$$

$$\frac{dN_{F_2}^{OUT}}{dt} = \beta_2^N H_2 N_Q^{OUT} - \sigma^N N_{F_2}^{OUT}$$

$$\frac{dA_Q^{IN}}{dt} = m^N \sigma^N N_{F_1}^{IN} - \beta_1^A H_1 A_Q^{IN} - d^A A_Q^{IN}$$

$$\frac{dA_{F_1}^{IN}}{dt} = \beta_1^A H_1 A_Q^{IN} + \rho A_{F_1}^{OUT} - \rho A_{F_1}^{IN} - \sigma_1^A A_{F_1}^{IN}$$

$$\frac{dA_Q^{OUT}}{dt} = m^N \sigma^N (N_{F_1}^{OUT} + N_{F_2}^{OUT}) - (\beta_1^A H_1 + \beta_2^A H_2) A_Q^{OUT} - d^A A_Q^{OUT}$$

$$\frac{dA_{F_1}^{OUT}}{dt} = \beta_1^A H_1 A_Q^{OUT} + scale \cdot \rho A_{F_1}^{IN} - scale \cdot \rho A_{F_1}^{OUT} - \sigma^A A_{F_1}^{OUT}$$

$$\frac{dA_{F_2}^{OUT}}{dt} = \beta_2^A H_2 A_Q^{OUT} - \sigma^A A_{F_2}^{OUT}.$$

Model for tick-borne infections without deer exclosure

$$\frac{dL_Q}{dt} = \frac{r^T}{1 + s^T T_{F_1}} \sigma^A A_{F_1} + \frac{r^T}{1 + s^T T_{F_2}} \sigma^A A_{F_2} - (\beta_1^L H_1 + \beta_2^L H_2)L_Q - d^L L_Q$$

$$\frac{dL_F^e}{dt} = \beta_1^L L_Q H_1^i + \beta_1^L L_Q (H_1^s + H_1^r)[1 - exp(-\lambda N_{F_1}^i / H_1)] - \sigma^L L_F^e$$

$$\frac{dL_F^s}{dt} = [\beta_1^L (H_1^s + H_1^r)exp(-\lambda N_{F_1}^i / H_1) + \beta_2^L H_2]L_Q - \sigma^L L_F^s$$

$$\frac{dN_Q^i}{dt} = m^L \sigma^L L_F^e - d^N N_Q^i - (\beta_1^N H_1 + \beta_2^N H_2)N_Q^i$$

$$\frac{dN_Q^s}{dt} = m^L \sigma^L L_F^s - d^N N_Q^s - (\beta_1^N H_1 + \beta_2^N H_2)N_Q^s$$

$$\frac{dN_{F_1}^i}{dt} = \beta_1^N H_1 N_Q^i - \sigma^N N_{F_1}^i$$

$$\frac{dN_{F_2}^i}{dt} = \beta_2^N H_2 N_Q^i - \sigma^N N_{F_2}^i$$

$$\frac{dN_F^e}{dt} = \beta_1^N N_Q^s H_1^i + \beta_1^N N_Q^s (H_1^s + H_1^r)[1 - exp(-\lambda N_{F_1}^i / H_1)] - \sigma^N N_F^e$$

$$\frac{dN_F^s}{dt} = [\beta_1^N (H_1^s + H_1^r)exp(-\lambda N_{F_1}^i / H_1) + \beta_2^N H_2]N_Q^s - \sigma^L N_F^s \qquad (3)$$

$$\frac{dA_Q^i}{dt} = m^N \sigma^N (N_{F_1}^i + N_{F_2}^i + N_F^e) - d^A A_Q^i - (\beta_1^A H_1 + \beta_2^A H_2)A_Q^i$$

$$\frac{dA_Q^s}{dt} = m^N \sigma^N N_F^s - d^A A_Q^s - (\beta_1^A H_1 + \beta_2^A H_2)A_Q^s$$

$$\frac{dA_F}{dt} = (\beta_1^A H_1 + \beta_2^A H_2)(A_Q^i + A_Q^s) - \sigma^A A_F$$

$$\frac{dH_1^s}{dt} = a_1(H_1)H_1 - d_1 H_1^s - \beta_1^N N_Q^i H_1^s$$

$$\frac{dH_1^i}{dt} = \beta_1^N N_Q^i H_1^s - (d_1 + \alpha + \gamma)H_1^i$$

$$\frac{dH_1^r}{dt} = \gamma H_1^i - d_1 H_1^r.$$

Tables

Table 1. Numerical values and biological interpretation of population parameters

Symbol	Description	Value (units)
r_1	Natural birth rate of rodents	0.00821 (day^{-1})
d_1	Natural death rate of rodents	0.0037 (day^{-1})
K_1	Carrying capacity of rodents	15 (ha^{-1})
H_2	Roe deer density	0.1 (ha^{-1})
r^T	Average egg production per fed adult tick	2000
s^T	Density-dependent death rate of ticks	0.25 (ha)
d^L	Death rate of larvae	0.0365 (day^{-1})
d^N	Death rate of nymphs	0.015 (day^{-1})
d^A	Death rate of adult ticks	0.00625 (day^{-1})
σ^L	Detachment rate of larvae	0.28 (day^{-1})
σ^N	Detachment rate of nymphs	0.22 (day^{-1})
σ^A	Detachment rate of adult ticks	0.12 (day^{-1})
m^L	Moulting success probability for larvae	0.15 (host^{-1} day^{-1})
m^N	Moulting success probability for nymphs	0.15 (host^{-1} day^{-1})
β_1^L	Encounter rate between questing larvae and rodents	0.015 (host^{-1} day^{-1})
β_1^N	Encounter rate between questing nymphs and rodents	0.0005 (host^{-1} day^{-1})
β_1^A	Encounter rate between questing adults and rodents	0.0001 (host^{-1} day^{-1})
β_2^L	Encounter rate between questing larvae and roe deer	0.2 (host^{-1} day^{-1})
β_2^N	Encounter rate between questing nymphs and roe deer	0.5 (host^{-1} day^{-1})
β_2^A	Encounter rate between questing adults and roe deer	0.5 (host^{-1} day^{-1})
λ	Co-feeding probability between infected and susceptible ticks	0.5 (host^{-1} day^{-1})
α	Disease-related death rate of rodents	0.1 (day^{-1})
γ	Recovery rate of rodent host	0.1 (day^{-1})

Figure legends

Fig. 1: Flow chart of models. Disregarding dashed lines, one has model (1); the symbols over the arrows represent the rate at which the transition occurs; the symbols in square brackets represent the conversion factor from one compartment to the next. Model (2) consists of 2 flow charts like this (with the one representing the inside compartment missing the L_{F_2}, N_{F_2} and A_{F_2} blocks) coupled by the dashed lines.

Fig. 2: Effect of rodent density (left panel) and deer density (right panel) on questing larvae and nymphs and feeding ticks on rodents. Parameter values are those reported in Tab. 1.

Fig. 3: Effect of the size of exclosure (ρ) on equilibria for feeding ticks on rodents inside (IN) and outside (OUT) the exclosure: larvae (top) nymphs (centre) and adult ticks (bottom). For simulations on the left (column *A*) β_2^L=0.05, β_2^N=0.03, β_2^A=0.13, while for simulations on the right (column *B*) β_2^L=0.2, β_2^N=0.5, β_2^A=0.5. In all simulations *scale*=0 while the other parameter values are those of Tab. 1.

Fig. 4: Temporal simulations for feeding nymphs on rodents after the introduction of exclosure. Two examples with different exclosure size: larger exclosure on left panel (ρ=0.05) and smaller exclosure on right panel (ρ=0.15). In both panels *scale*=0 while the other parameter values are those of Tab. 1.

Fig. 5: Effect of rodent density (left panel) and deer density (right panel) on the equilibrium levels of questing infected nymph density, and of TBE seroprevalence in rodents. Parameter values are those reported in Tab. 1.

Fig. 6: Effect of the size of exclosure (ρ) on equilibrium for questing infected nymph density (left) and TBE seroprevalence in rodents (right) inside and outside the exclosure. In both panels *scale*=0 while the other parameter values are those of Tab. 1.
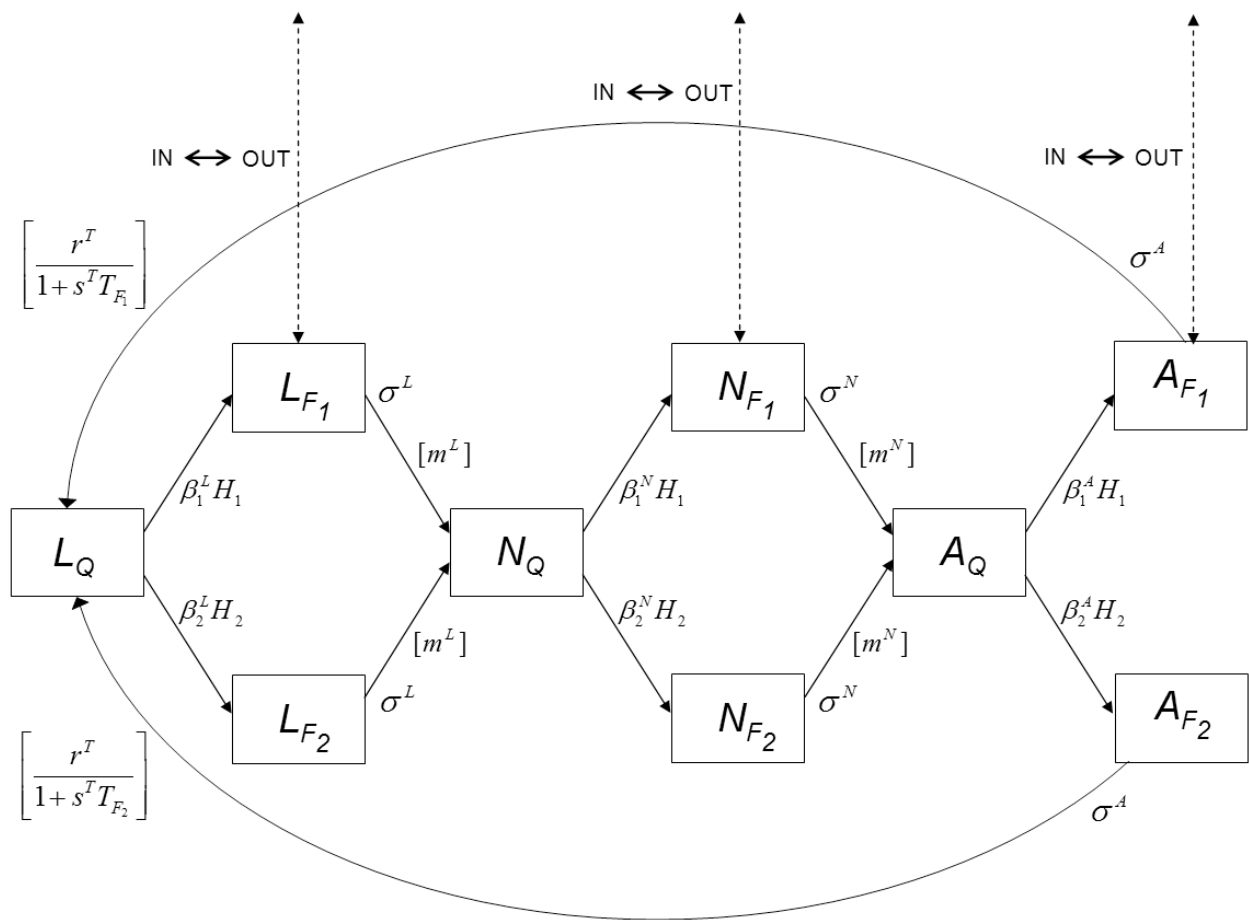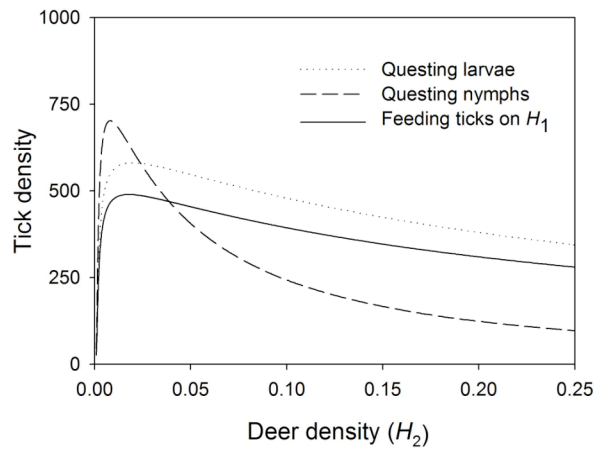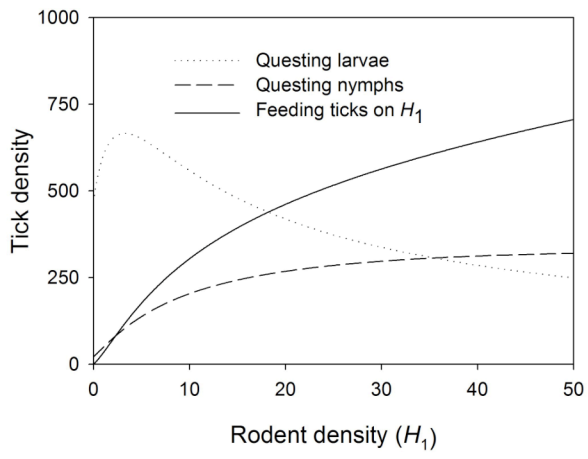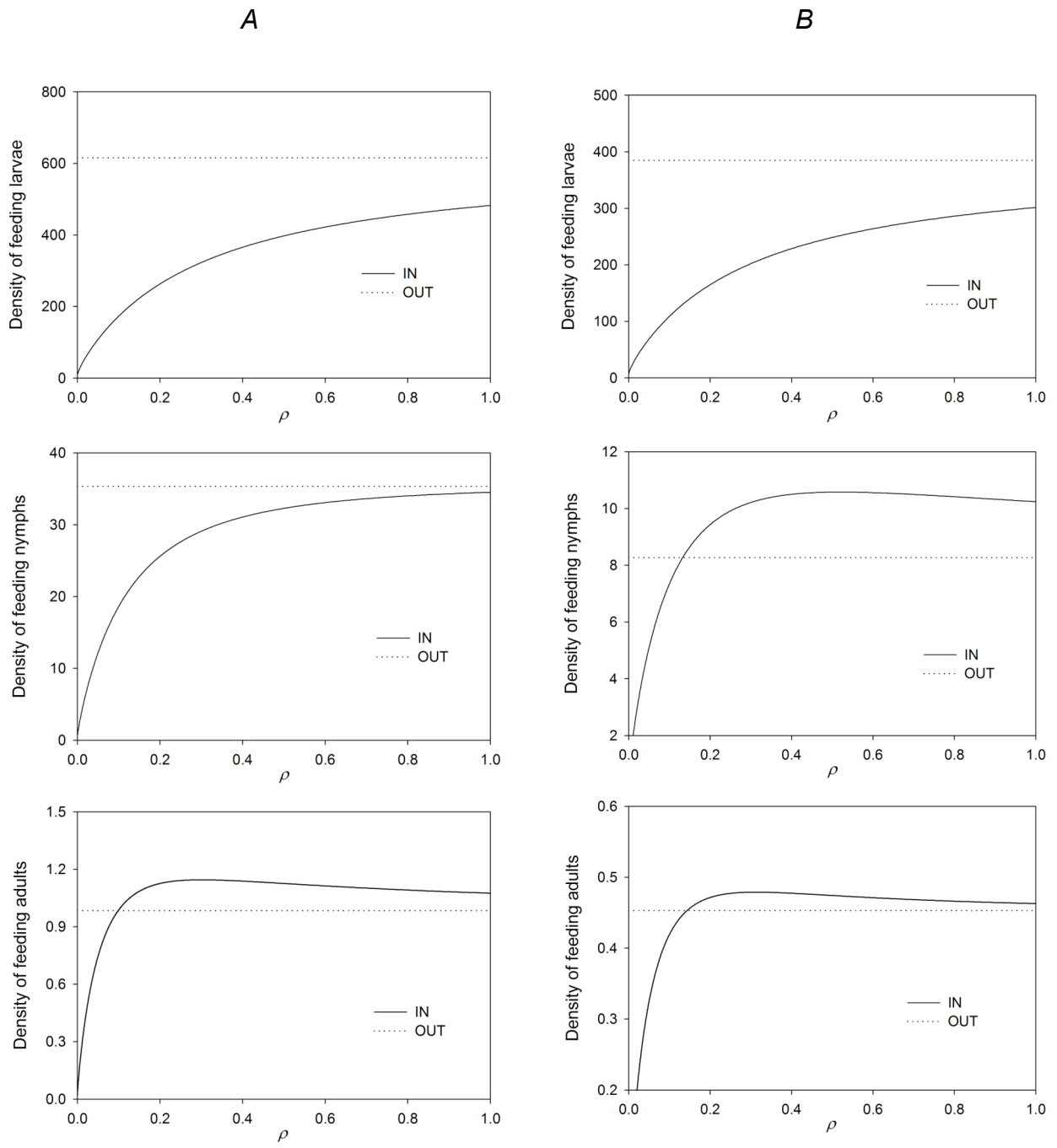
$$\left[\dfrac{r^T}{1+s^T T_{F_1}}\right]$$

IN ⟷ OUT

IN ⟷ OUT

IN ⟷ OUT

σ^A

L_{F_1} σ^L

N_{F_1} σ^N

A_{F_1}

$[m^L]$

$[m^N]$

$\beta_1^L H_1$

$\beta_1^N H_1$

$\beta_1^A H_1$

L_Q

N_Q

A_Q

$\beta_2^L H_2$

$\beta_2^N H_2$

$\beta_2^A H_2$

$[m^L]$

$[m^N]$

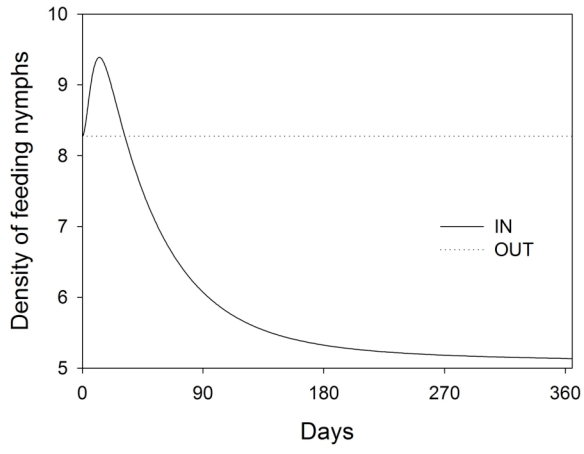L_{F_2} σ^L

N_{F_2} σ^N

A_{F_2}

$$\left[\dfrac{r^T}{1+s^T T_{F_2}}\right]$$

σ^A

Figure 1

Figure 2

Figure 3
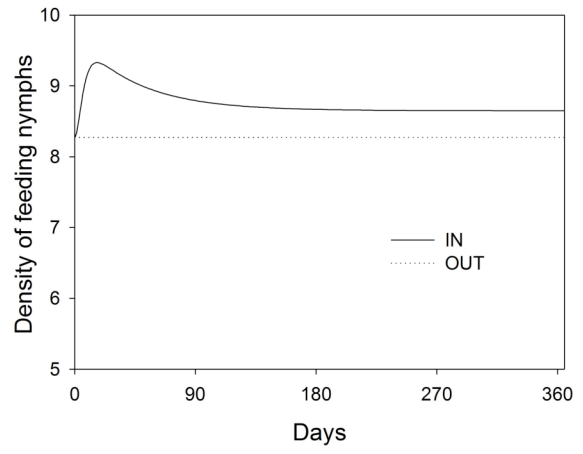
Figure 4

Figure 5

Figure 6