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The role of non-viraemic transmission on the persistence and dynamics of a tick borne virus – Louping ill in red grouse (*Lagopus lagopus scoticus*) and mountain hares (*Lepus timidus*)

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Abstract. There exist many tick borne infections that are of either economic or public health interest. Mathematical models have previously been used to describe the dynamics of these infections. However it has recently come to light that there is an alternative mechanism for the transmission of these diseases that has not been considered in a modelling framework. This is transmission through ticks co-feeding on non-viraemic hosts. This paper extends a simple mathematical model to include this alternative transmission mechanism. The model is used to describe the dynamics of Louping ill virus in red grouse (the viraemic host) and hares (the non-viraemic host). However, these results are applicable to many other systems. The model is analysed using joint threshold density curves. It is found that the presence of a non-viraemic host allows the virus to persist more readily than it would in the presence of a host that simply amplified the tick population. More importantly, if the level of non-viraemic transmission is high enough the virus can persist in the absence of the viraemic host. This result has important implications for the control of tick borne diseases.

Introduction

Tick borne–viruses are known to have a significant impact on human, livestock and wild animal populations in the tropical and temperate parts of the world (Sonenshine and Mather 1994). However, the dynamics of infection are complicated in tick borne virus systems since ticks feed on a wide range of host species and efficiency of transmission from host to tick and tick to host varies between host species.

Transmission from host to tick is generally believed to occur when ticks bite and feed on the blood of a viraemic host (e.g. Beasley et al 1978). However, in recent years it has become clear that pathogen transmission can occur through a

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number of other routes. For example transmission between infected and uninfected ticks that co-feed on a host can occur in the absence of systemic infection (Jones et al 1987). This has been shown to occur for both viruses and bacteria (Randolph et al 1996). There is evidence that this transmission occurs due to host modification at the feeding site and is facilitated by tick saliva (Jones et al 1992, Labuda et al 1993a). However, non-viraemic transmission does not occur on all host species. For example, in the Louping ill system it has been shown to occur on Mountain hares (*Lepus timidus*) but transmission has not been recorded on red deer (*Cervus elaphus*), New Zealand white rabbits or domestic sheep although further investigation is still needed (Jones et al 1997). Furthermore, non viraemic transmission has also been observed in mountain hares after sero - conversion implying that such hosts may provide suitable habitat for transmission for much longer than normal viraemic hosts. Indeed if such hosts are relatively abundant they could provide the main route of virus transmission and be the principal mechanism for virus persistence.

A number of mathematical models have been formulated to describe transmission of tick borne diseases through the normal systemic route (e.g. Cooksey et al 1990, O'Callaghan et al 1998, Norman et al 1999). However, such models have not included the non-viraemic transmission route so the aim of this paper is to incorporate this transmission mechanism. Specifically we will address three questions:

- 1) How does non-viraemic transmission alter the dynamics of infection?
- 2) How does it influence virus persistence?
- 3) Are these results applicable to other systems?

Whilst non-viraemic transmission has now been recorded in several different systems (e.g. Labuda et al 1993b, Jones et al 1990), we will concentrate initially on our system; Louping ill virus which has two viraemic hosts, red grouse (*Lagopus lagopus scoticus*) and sheep and where non- viraemic transmission occurs in Mountain Hares (*Lepus timidus*) (Jones et al 1997).

Louping ill

Louping ill is a tick borne virus transmitted by the sheep tick *Ixodes ricinus*. Whilst the tick bites a wide variety of hosts it is only in sheep, grouse and 2% of short tailed voles that the virus invokes a viraemic response sufficiently high for ticks to become infected through the systemic route of infection (Hudson et al 1995). Although Louping ill has economic implications for sheep farmers it is usually controlled in sheep by vaccination and regular treatment with acaricides. Grouse, on the other hand, suffer substantial losses from the disease with 80% of those infected with the virus dying (Reid 1978, Hudson 1992). These huge losses coupled with the fact that adult ticks do not feed on grouse should mean that, if sheep are effectively removed from the system through vaccination and dipping, then the virus would not persist. In a number of areas, the disease in grouse has been reduced through sheep management. However, Louping ill is still prevalent in some parts of Scotland despite applying sheep management procedures. Persistence of the virus could occur for several possible reasons that are explored by Hudson et al 1995. In

their study they provide evidence to suppose that the presence of the mountain hares plays an important role in the persistence of Louping ill virus. This could operate in a combination of one or two ways. First hares could act as a maintenance host for the tick vectors and this could allow virus persistence. A generalised mathematical model of tick borne viruses which included a viraemic host and a secondary tick host that simply allowed adult feeding of ticks showed that for medium densities of the non-viraemic host, the virus could persist in areas where it would not persist in the presence of the viraemic hosts alone (Norman et al 1999). This modelling also showed that if non-viraemic host abundance is too high this could result in the virus being lost from the system through wasted bites (Norman et al 1999). We now extend this model to incorporate recent experimental work that shows that hares can act as non-viraemic hosts to Louping ill, permitting the virus to be transmitted between co-feeding ticks (Jones et al 1997).

The approach in this paper is to present a simple deterministic model for the transmission of the virus which causes Louping ill. We parameterise this model for the Louping ill system before analysing the model output in terms of the possible implications of non-viraemic transmission in the Louping ill system.

Biological Assumptions of the model

The dynamics of the tick vector are based on the biology of the tick *Ixodes ricinus* that transmits the virus that causes Louping ill. This tick has a life cycle that develops from the egg through two immature stages (larva and nymph) to the adult stage. Each immature stage requires a blood meal from a suitable vertebrate host. The adult female requires a meal before producing eggs once and then dying. Adult females can only obtain a feed from large mammals i.e. hares and not grouse, whilst the immature stages will also feed on smaller warm-blooded vertebrates such as grouse chicks. Once a questing tick locates a host it generally feeds for several days. The tick life cycle usually takes 3 to 4 years but can be longer depending on host availability and climatic conditions, ticks need high relative humidity to survive.

Low tick burdens do not have a direct impact on the host (Hudson 1986, 1992). However, the virus is transmitted inter-stadially so once an immature stage is infected the subsequent stages can transmit the virus to a susceptible host. Transovarial transmission has not been recorded in the Louping ill system.

We assume that sheep play no part in the dynamics of the system and have been effectively removed through vaccination and acaricide treatment.

The model

The model presented here considers two hosts, a viraemic host that does not support adult ticks and a non-viraemic host that supports all stages. We call these hosts grouse (G) and hares (H) respectively. Grouse are assumed to be susceptible (s), infected (i) or immune (z) with total grouse density, $G = G_s + G_i + G_z$. Hares are assumed to be at a constant density H. For simplicity the tick stages are added to give two equations for the tick dynamics, one for infected ticks (T_i) and one for

susceptible ticks (T_s) with the total tick population, $T = T_i + T_s$. Despite this addition of tick stages the parameters values used are calculated in a way which only accounts for the specific tick stages which are involved in a particular mechanism. The model is an extension of the viraemic transmission model analysed previously by (Norman et al 1999). The rate of non-viraemic transmission is assumed to be proportional to the number of hares present, the number of infected ticks present and the number of susceptible ticks present and therefore takes the form $\theta HT_i T_s$ where θ is a measure of the probability of non-viraemic transmission occurring. This is obviously a simple relationship and a more realistic one may be required to describe the aggregated distribution of ticks. However, we do not currently have the data available to support any such relationship and so we will start with the simplest one possible. The equations that describe the system are therefore as follows:

$$\frac{dG_s}{dt} = (a_g - s_g G)G - b_g G_s - \beta_1 T_i G_s \quad (1)$$

$$\frac{dG_i}{dt} = \beta_1 T_i G_s - \Gamma G_i \quad (2)$$

$$\frac{dG_z}{dt} = \gamma G_i - b_g G_z \quad (3)$$

$$\frac{dT_s}{dt} = (a_T - s_T T)T\beta_3 H - b_T T_s - \beta_2 T_s G_i - \theta T_i T_s H - \beta_3 T_s H \quad (4)$$

$$\frac{dT_i}{dt} = \theta T_i T_s H + \beta_2 T_s G_i - b_T T_i - \beta_3 T_i H \quad (5)$$

Where for grouse: a_g is the per capita birth rate; s_g is a measure of the density dependent constraints acting on the birth rate of the population; b_g is the per capita natural death rate; β_1 is the probability of an average tick biting a grouse and infecting it per unit time; γ is the rate at which infectious grouse become immune and $\Gamma = \alpha + b_g + \gamma$ is the rate at which infectious grouse are lost from the system and is the sum of the death rate due to the disease (α), the natural death rate and the rate at which individuals become immune. For the ticks: a_T is the per capita production rate of larvae; s_T is a measure of the density dependence acting on tick production rate; b_T is the per capita natural death rate. β_2 is the probability of an average tick biting a grouse and becoming infected per unit time; β_3 is the probability of an adult tick being female, biting a hare and then going on to reproduce per unit time before dying and being lost from the system. A measure of non-viraemic transmission is given by θ . In order to calculate the value of θ we really need to take into account the probabilities of susceptible and infected ticks co-feeding on a hare either spatially or temporally and, in addition, the probabilities of infection.

Parameter estimation

The parameters for the grouse-hare- Louping ill system are estimated from data in the literature and from our current unpublished results (Table 1). All parameters are calculated per month and we ignore seasonality in this simple model. Some of the life history parameters are relatively trivial to calculate. For example, to calculate the per capita reproductive rate of grouse, a_g , we assume that breeding pairs of grouse have, on average four chicks per year (Hudson 1992), ignoring singletons, this gives a productivity of 2 chicks per bird per year which is $2/12 = 0.166$ chicks per bird per month and hence $a_g = 0.166$. We estimate α from the observation that it takes approximately 13 days for a grouse to die from Louping ill (Reid 1975) and so the death rate due to the disease, $\alpha = 30/13 = 2.31$ per month (assuming 30 days per month). Since 80% of infected grouse die from the disease (Reid 1978, Hudson 1992) then γ is 4 times smaller than α therefore $\gamma = 0.5775$. The transmission parameters are not so easy to measure. The β s are defined as the probability of an average tick biting an average host and infection occurring per unit time. This is difficult to estimate, however we do have information on tick biting rates on both hares and grouse on a major study area in Scotland for the years 1993, 1994 and 1995. In order to estimate the β s we make the simplifying assumptions that the ratio of larvae to nymphs to adults remains constant and the ratio of ticks biting hares to ticks biting grouse remains constant. We also assume that the probabilities of infection remain constant across tick life stages and across host species. The transmission parameters are defined as follows:

β_1 is the probability of an average infectious tick biting an average grouse and infecting it within a unit time. This can only occur within the nymph stage since adult ticks do not usually bite grouse. β_2 is the probability of an average tick biting an infected grouse and becoming infected so both larvae and nymphs contribute to this term. β_3 is the probability of an average female adult biting a hare and subsequently producing eggs and then larvae and takes into account the proportion of the tick population which is female. We can therefore rewrite the biting rates as $\beta_1 = \beta$, $\beta_2 = p\beta$ and $\beta_3 = q\beta$. Using the data on tick biting rates described above,

Table 1. Parameter definitions, estimates and their sources.

Parameter	Meaning	Value per month	Source
a_g	Per capita birth rate for grouse	0.166	Hudson 1992
b_g	Per capita natural death rate of grouse	0.087	Jenkins et al 1967 Hudson, 1992
α	Death rate due to the disease	2.31	Reid 1975
γ	Rate of recovery from the disease	0.5775	Calculated from α
a_r	Number of larvae produced per tick	83.33	Unpublished data
b_r	Natural death rate of ticks	0.0277	Unpublished data

we estimate that $p = 2.525$ and $q = 1.13$. This leaves us with the single parameter, β , to estimate and we analyse the model for several different values of this parameter. Another parameter for which we have no estimate is the non-viraemic transmission parameter θ . Again, we consider several values of this parameter to study the possible effects of non-viraemic transmission in virus persistence.

Model analysis

Setting the derivatives of equations (1) to (5) to zero we find that there are six possible biologically relevant equilibria (see appendix A). Details of the stability analyses of these equilibria are given in appendix B.

The trivial equilibrium has no grouse, ticks or disease present and is only stable if $a_g < b_g$ and $a_T \beta_3 H < b_T + \beta_3 H$ in other words if the death rate of both species is higher than their birth rates. One way of interpreting the second inequality is as the basic reproductive number of the ticks, $R_{o,ticks} < 1$ where

$$R_{o,ticks} = \frac{a_T \beta_3 H}{b_T + \beta_3 H}$$

$R_{o,ticks}$ can be derived directly from the equations. If we add equations (4) and (5) we see that if one tick was added to an area that had H hosts then it would live for $\frac{1}{b_T + \beta_3 H}$ units of time and produce $a_T \beta_3 H$ offspring per unit time and so in its lifetime the initial tick would produce

$$R_{o,ticks} = \frac{a_T \beta_3 H}{b_T + \beta_3 H}.$$

The next simple case is no grouse and ticks all susceptible and at their carrying capacity. This equilibria is only stable if $a_g < b_g$, $a_T \beta_3 H > b_T + \beta_3 H$ ($R_{o,ticks} > 1$) and $\theta K_T H < b_T + \beta_3 H$ in other words if the grouse population has a negative growth rate, the tick population has a positive growth rate and the disease cannot be spread non-viraemically because ticks die more quickly than they can become infected through this route.

The third equilibria has no ticks present, no disease and grouse present at their carrying capacity. This equilibria is stable, as we might expect, when $a_g > b_g$ and $R_{o,ticks} < 1$ i.e. the grouse have a positive growth rate and the ticks have a negative one. The fourth equilibria has ticks and grouse both at their carrying capacities and no infection. This equilibria is stable if $a_g > b_g$, $R_{o,ticks} > 1$ and $R_{o,virus} < 1$ where

$$R_{o,virus} = \frac{\theta H K_T \Gamma + \beta_2 K_T \beta_1 K_g}{\Gamma(b_T + \beta_3 H)}$$

Again we can derive this formula from equations (1)–(5). Consider a system in which grouse are at their carrying capacity K_g , ticks are at their carrying capacity K_T and hares are at density H . If we add one infected tick to this system $R_{o,virus}$ is the number of secondarily infected ticks caused by this primary infection. From equation (5) the tick would live for $\frac{1}{b_T + \beta_3 H}$ units of time and produces $\frac{\beta_1 K_g}{b_T + \beta_3 H}$ infected grouse through feeding and $\frac{\theta K_T H}{b_T + \beta_3 H}$ infected ticks through co-feeding. Each

infected grouse lives for $\frac{1}{\Gamma}$ units of time and produces $\frac{\beta_2 K_T}{\Gamma}$ infected ticks. Adding these two routes of infection together gives

$$R_{o,virus} = \frac{\beta_2 K_T \beta_1 K_g}{\Gamma(b_T + \beta_3 H)} + \frac{\theta K_T H}{b_T + \beta_3 H}$$

The next equilibrium is one with no grouse present and ticks at their carrying capacity but with infection. This is stable if $a_g < b_g$, $R_{o,ticks} > 1$ and $\theta K_T H > b_T + \beta_3 H$ in other words if the grouse population has a negative growth rate, the tick population has a positive growth rate and the disease can be spread non-viraemically. The third inequality can be derived from the formula for $R_{o,virus} > 1$, given above, with $K_g = 0$.

The sixth and final equilibrium has grouse, ticks and virus all present and is assumed to be stable (or replaced by cycles) when $a_g > b_g$, $R_{o,ticks} > 1$ and $R_{o,virus} > 1$. Numerical simulations support this assumption.

If we first consider $R_{o,ticks}$ we see that it is not dependent on grouse density, this is because tick reproduction depends purely on hares since adult ticks do not bite grouse. Putting $R_{o,ticks} = 1$ gives us a threshold density of hares, H_T , below which the ticks cannot persist where,

$$H_T = \frac{b_T}{(a_T - 1)\beta_3}$$

For this threshold to be low, i.e. for ticks to persist easily we need a low natural tick death rate, a high tick birth rate and high biting rates for adult females.

In order to consider the effects of hares on the persistence of the virus which causes Louping ill we plot the curves $R_{o,virus} = 1$ in grouse-hare (K-H) parameter space. We can identify the areas in parameter space in which the virus can and cannot persist. If we first consider the system without non-viraemic transmission then we have two parameter values for which we do not have estimates these are β and s_T so we vary these to see how the behaviour of the system is affected. If we keep s_T constant and vary β (Figure 1) we find that for large β the curve bends back upon itself. This means that for a given value of grouse carrying capacity, K_g , there are two threshold values of H. If there are too few hares then the life cycle of the ticks cannot be completed so there are too few ticks for the virus to persist. If there are too many hares then, since there is no non-viraemic transmission in this case, the bites on hares are wasted in terms of the virus which becomes diluted in the tick population and dies out. For smaller values of β the curve no longer bends back on itself and this dilution effect disappears. It should be noted that for larger values of β the grouse carrying capacities for which the virus cannot persist are very low and it is unlikely that these values of β are realistic. For smaller values of β whilst the dilution effect has disappeared we need much higher densities of hares and grouse present before the virus can persist.

If we vary s_T we find that the curve does not change shape but moves along the K_g axis making persistence of the disease more or less likely depending on whether s_T is increased or decreased. (Figure 2). These changes in the threshold grouse carrying capacities are proportional to changes in s_T , in other words if s_T

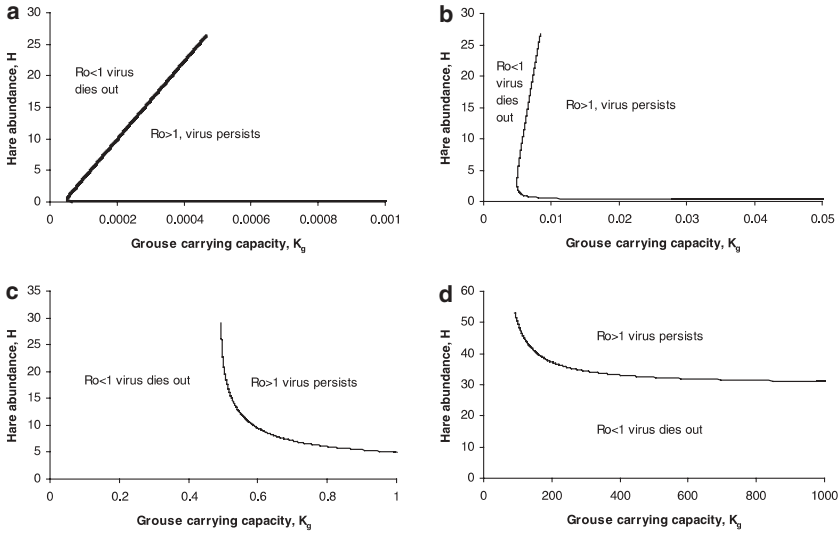


Fig. 1. Relationship between $R_{o,virus} = 1$ for four different values of β . All other parameter values are as in Table 1 and $s_T = 0.00001$. In figure 1a $\beta = 0.01$ and the threshold level of hares, H_T below which the ticks cannot persist is 0.0298. In figure 1b $\beta = 0.001$ and $H_T = 0.298$. In figure 1c $\beta = 0.0001$ and $H_T = 2.98$ and in figure 1d $\beta = 0.00001$ and $H_T = 29.8$.

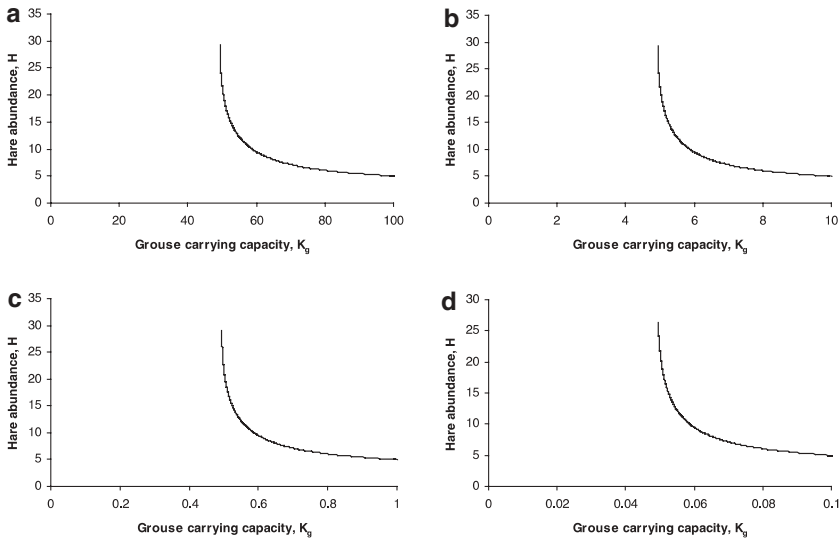


Fig. 2. Graphs to show the effect of changing s_T on the persistence of the virus. In each case parameters are as in Table 1 and $\beta = 0.0001$. In figure 2a $s_T = 0.001$, in figure 2b $s_T = 0.0001$, in figure 2c $s_T = 0.00001$ and in figure 2d $s_T = 0.000001$.

is decreased by a factor of 10 then we need 10 times fewer grouse for persistence. This is because when s_T is smaller then the carrying capacity of ticks is larger and so transmission is more likely.

We now add in non-viraemic transmission. In this case we have no available estimates for the value of θ and so we take different values and see the effect of this parameter on system behaviour. We consider two values of β and look at the effect of increasing θ (Figure 3 and 4). Since $R_{o,ticks}$ does not depend on θ we find that H_T does not change when we add non-viraemic transmission. In terms of virus persistence we find that adding non-viraemic transmission to the model makes the virus more likely to persist. This is mainly seen at low grouse carrying capacities. With the addition of non-viraemic transmission the dilution effect completely disappears. Indeed the curve now crosses the ‘Hare’ axis, this means that, for high enough non-viraemic transmission, even if an area could not support grouse then the virus could persist if there were enough hares, this result is confirmed by the stability analysis (equilibrium 5, Appendix A). One point of interest is the point at which the $R_{o,virus}$ curve crosses the hare axis and how this is influenced by the amount of non-viraemic transmission occurring. If we assume that grouse cannot be sustained in an area, as shown above, we find $R_{o,virus} = \frac{\theta K_T \bar{H}}{b_T + \beta_3 \bar{H}}$. Setting $R_{o,virus} = 1$ and rearranging we can find the threshold number of hares which have to be present for virus persistence in this area. This gives us

$$H = \frac{b_T}{\theta K_T - \beta_3}$$

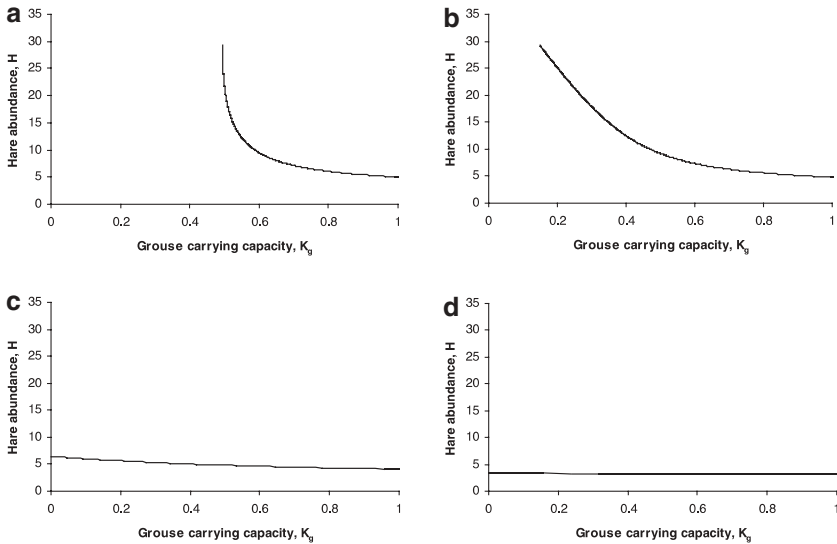


Fig. 3. Graphs to show the effect of non-viraemic transmission on the persistence of the virus. In each case the parameters are as in Table 1 with $s_T = 0.00001$ and $\beta = 0.0001$. In figures 3a to 3d θ takes the values 0 , 1×10^{-10} , 1×10^{-9} and 1×10^{-8} respectively.

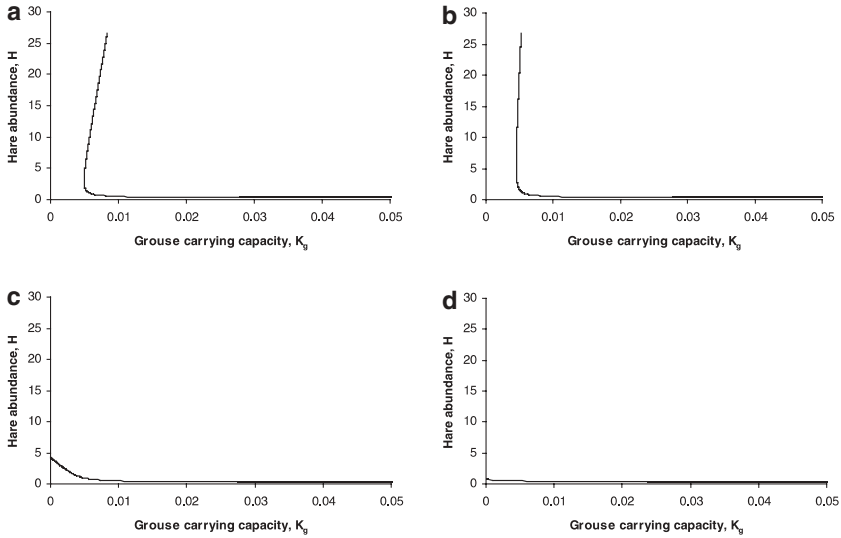


Fig. 4. Graphs to show the effect of non-viraemic transmission on the persistence of the virus. In each case the parameters are as in Table 1 with $s_T = 0.00001$ and $\beta = 0.001$. In figures 4a to 4d θ takes the values 0 , 1×10^{-10} , 1×10^{-9} and 1×10^{-8} respectively.

It is clear that the hare threshold density is lowered if either the ticks are long lived or non-viraemic transmission is more likely to occur.

Discussion

Tick borne diseases are of increasing importance in terms of their economic and health implications. Some headway has been made in controlling some of these diseases through vaccination and acaricide treatments. However, it has recently come to light that alternative mechanisms of transmission occur which might make control of these viruses more difficult. One method that could be of particular importance is non-viraemic transmission. This is known to occur in several systems and involves transmission of the virus from an infected tick to a susceptible one when they co-feed either spatially or temporally on a host that does not produce a viraemic response (Randolph et al 1996). This paper has used mathematical models to consider the possible effects of non-viraemic transmission on the persistence of the virus.

We concentrated specifically on the Louping ill system in which we have two hosts, red grouse which produce a viraemic response and mountain hares which do not. A previous model of tick borne diseases in general (Norman et al 1999) has shown that the presence of a non-viraemic hosts could amplify the tick population enough to cause persistence of the virus in areas where it could not persist in the absence of these hosts. However, it is also possible for too many non-viraemic hosts to be present for virus persistence since a ‘dilution effect’ occurs where tick bites are wasted and the virus dies out (Norman et al 1999). These results are shown here to be true, for some levels of virus transmission, for parameters that describe

the Louping ill system. However, these levels of transmission are unlikely to be realistic and it appears that the dilution effect is not important in the Louping ill system. The effect of non-viraemic transmission, if it occurs frequently enough, is to remove any dilution effect that does occur and to generally increase the probability that the virus can persist, particularly at low grouse carrying capacities. Indeed, if the non-viraemic transmission parameter and hare densities were both high enough it would be possible for the hares to sustain the virus in areas where grouse are unable to persist. Unfortunately we do not yet have any idea of the levels of non-viraemic transmission that occur in the field. However, this work suggests that non-viraemic transmission could be of great significance in virus persistence in the grouse-hare-Louping ill system.

Whilst the model results here are given for the Louping ill system the model presented could be applied to any tick borne virus system in which we have both a viraemic host and a non-viraemic host simply by changing the parameter values. Other systems for which non-viraemic transmission is known to occur include tick-borne encephalitis (Labuda et al 1993b), Lyme disease (Ogden et al 1997) and Thogoto virus (Jones et al 1990). Whilst we do not have estimates for the level of non-viraemic transmission occurring in these systems there is evidence in the Lyme disease system that it is significant. Recent work has shown that although sheep do not develop systemic infections Lyme disease cycles can be maintained in habitats dominated by sheep (Ogden et al 1997). Whilst this does not validate the model results it does provide evidence that they are biologically realistic.

Whilst the model presented here is very simple it produces a result which has serious implications for disease control. That is, that we cannot simply consider viraemic hosts when we are thinking about the control of tick borne viruses. We also have to find out if the system has any non-viraemic hosts and consider ways of removing them from the transmission cycle as well. This will be made difficult by the fact that we will not be able to vaccinate against the virus in order to bring about this removal since non-viraemic transmission can occur even if an immune response has been mounted.

Appendix A: Equilibria

The biologically relevant equilibria for equations (1)–(5) are found by setting the derivatives equal to zero. We then get the following equilibria, written in the form $(G_s, G_i, G_z, T_s, T_i)$.

- 1) $(0, 0, 0, 0, 0)$, i.e. no grouse, ticks or disease present.
- 2) $(0, 0, 0, K_T, 0)$, i.e. no grouse or disease and ticks at their carrying capacity, K_T , which is given by

$$K_T = \frac{a_T \beta_3 H - b_T - \beta_3 H}{s_T \beta_3 H}.$$

For this to be biologically relevant (i.e. positive) we need

$$a_T \beta_3 H > b_T + \beta_3 H.$$

- 3) $(K_g, 0, 0, 0, 0)$, i.e. no ticks or disease and grouse at their carrying capacity, K_g , which is given by

$$K_g = \frac{r_g}{s_g}$$

For this to be biologically relevant we need

$$r_g > 0 \text{ i.e. } a_g > b_g$$

- 4) $(K_g, 0, 0, K_T, 0)$, i.e. grouse and ticks both at their carrying capacity with no disease present. Here K_g and K_T are as given above and for this equilibrium to be biologically relevant we need both

$$a_T \beta_3 H > b_T + \beta_3 H \text{ and } a_g > b_g$$

- 5) $(0, 0, 0, T_s^+, T_i^+)$, i.e. no grouse present but ticks and disease coexisting. In this case

$$T_s^+ = \frac{b_T + \beta_3 H}{\theta H}, \text{ which is always positive and}$$

$$T_i^+ = K_T - \frac{b_T + \beta_3 H}{\theta H}, \text{ which is only biologically relevant when}$$

$$\theta H K_T > b_T + \beta_3 H.$$

- 6) $(G_s^*, G_i^*, G_z^*, T_s^*, T_i^*)$, i.e. ticks, grouse and disease coexisting together. This equilibrium is much more complicated than those above and is given by the following formulae:

$$G^* = \frac{1}{s_g} \left(\frac{b_g \Gamma}{b_g \Gamma + (b_g + \gamma) \beta_1 T_i^*} \right) \left(a_g \left(\frac{b_g \Gamma + (b_g + \gamma) \beta_1 T_i^*}{b_g \Gamma} \right) - b_g - \beta_1 T_i^* \right)$$

with

$$G_s^* = \frac{b_g \Gamma G^*}{b_g \Gamma + (b_g + \gamma) \beta_1 T_i^*}, G_i^* = \frac{\beta_1 T_i^* G_s^*}{\Gamma}, \text{ and } G_z^* = \frac{\gamma \beta_1 T_i^* G_s^*}{b_g \Gamma}.$$

The total tick population T is equal to K_T , which has the same formula as given above. The susceptible tick density is given by $K_T - T_i^*$. Hence, we can write all of the densities in terms of the infectious tick density, T_i^* . However, T_i^* is given by the following cubic:

$$f(T_i^*) = AT_i^{*3} + BT_i^{*2} + CT_i^* + D$$

where

$$A = \theta H s_g (b_g + \gamma)^2 \beta_1^2$$

$$B = -\theta K_T H s_g (b_g + \gamma)^2 \beta_1^2 + 2\theta H s_g (b_g + \gamma) \beta_1 \Gamma b_g + \beta_2 \beta_1^2 b_g a_g (b_g + \gamma) - \beta_2 \beta_1^2 b_g^2 \Gamma + (b_T + \beta_3 H) s_g (b_g + \gamma)^2 \beta_1^2$$

$$C = -2\theta H \Gamma s_g b_g (b_g + \gamma) \beta_1 K_T + \theta H \Gamma^2 s_g b_g^2 - \beta_2 K_T \beta_1^2 b_g a_g (b_g + \gamma) + \beta_2 K_T \beta_1^2 \Gamma b_g^2 + \beta_2 \beta_1 \Gamma b_g^2 a_g - \beta_2 \beta_1 \Gamma b_g^3 + 2\beta_1 \Gamma s_g b_g (b_g + \gamma) (b_T + \beta_3 H)$$

$$D = -\theta H K_T s_g \Gamma^2 b_g^2 - \beta_2 K_T \beta_1 \Gamma b_g^2 a_g + \beta_2 K_T \beta_1 \Gamma b_g^3 + \Gamma^2 b_g^2 s_g (b_T + \beta_3 H)$$

In order to determine the properties of this cubic we will look at $f(0)$ and $f(K_T)$.

$$f(0) = D = b_g^2 \Gamma s_g (\Gamma (b_T + \beta_3 H) - \theta H K_T \Gamma - \beta_2 \beta_1 K_T K_g)$$

This is negative if $R_{0,virus} > 1$ and hence we have either 1 or three positive roots.

$$f(K_T) = b_T r_g (b_g + \gamma)^2 \beta_1^2 K_T^2 + \beta_3 H r_g (b_g + \gamma)^2 \beta_1^2 K_T^2 + 2b_T r_g \Gamma b_g (b_g + \gamma) \times \beta_1 K_T + 2\beta_3 H r_g \Gamma b_g (b_g + \gamma) \beta_1 K_T + (b_T + \beta_3 H) r_g \Gamma^2 b_g^2$$

which is positive as long as $r_g > 0$. This means that there is at least one root between 0 and K_T and there may be three. Therefore, as long as $R_{0,virus} > 1$ and $r_g > 0$ there is always at least one positive value for T_i^* . If T_i^* is positive it is easy to show that the other terms in the equilibrium are positive and so the coexistence equilibrium exists. However, it has not been possible to show algebraically that this equilibrium is unique, however, to date no numerical solutions of this system have shown more than one positive coexistence equilibrium.

Appendix B: Stability

In order to check the local stability of the six biologically relevant equilibria described in appendix A we follow a standard method of analysis (Anderson and May 1981). This is to perturb the system away from each equilibrium, and determine the conditions under which it returns to the same equilibrium. This is done by determining the eigenvalues of the Jacobian evaluated at each equilibrium. If the eigenvalues have negative real parts then the equilibrium is stable.

The general form of the Jacobian is as follows:

$$\begin{pmatrix} a_g - 2s_g G - b_g - \beta_1 T_i & a_g - 2s_g G & a_g - 2s_g G & 0 & -\beta_1 G_s \\ \beta_1 T_i & -\Gamma & 0 & 0 & \beta_1 G_s \\ 0 & \gamma & -b_g & 0 & 0 \\ 0 & -\beta_2 T_s & 0 & a_T \beta_3 H - 2s_T T \beta_3 H - b_T & a_T \beta_3 H - 2s_T T \beta_3 H - \theta T_s H \\ 0 & \beta_2 T_s & 0 & -\beta_2 G_i - \theta T_i H - \beta_3 H & \theta T_i H + \beta_2 G_i \\ & & & & \theta T_s H - b_T - \beta_3 H \end{pmatrix}$$

1) At $(0, 0, 0, 0, 0)$ the eigenvalues of the Jacobian are given by

$$\begin{vmatrix} a_g - b_g - \lambda & a_g & a_g & 0 & 0 \\ 0 & -\Gamma - \lambda & 0 & 0 & 0 \\ 0 & \gamma & -b_g - \lambda & 0 & 0 \\ 0 & 0 & 0 & a_T \beta_3 H - b_T - \beta_3 H - \lambda & a_T \beta_3 H \\ 0 & 0 & 0 & 0 & b_T - \beta_3 H - \lambda \end{vmatrix} = 0$$

The solutions of this are $a_g - b_g$, $-\Gamma$, $-b_g$, $-b_T - \beta_3 H$ and $a_T \beta_3 H - b_T - \beta_3 H$. Therefore this equilibrium is stable iff $b_g > a_g$ and $b_T + \beta_3 H > a_T \beta_3 H$, in other words if death rates are higher than birth rates for both grouse and ticks.

2) At $(0, 0, 0, K_T, 0)$ the eigenvalues of the Jacobian are given by

$$\begin{vmatrix} a_g - b_g - \lambda & a_g & a_g & 0 & 0 \\ 0 & -\Gamma - \lambda & 0 & 0 & 0 \\ 0 & \gamma & -b_g - \lambda & 0 & 0 \\ 0 & -\beta_2 K_T & 0 & a_T \beta_3 H - 2s_T K_T \beta_3 H - b_T - \beta_3 H - \lambda & a_T \beta_3 H - 2s_T K_T \beta_3 H - \theta K_T H \\ 0 & \beta_2 K_T & 0 & 0 & \theta K_T H - b_T - \beta_3 H - \lambda \end{vmatrix} = 0$$

The solutions of this are $a_g - b_g, -\Gamma, -b_g, -s_T K_T \beta_3 H$ and $\theta K_T H - b_T - \beta_3 H$. Therefore this equilibrium is stable iff $b_g > a_g, K_T > 0$ i.e. $b_T + \beta_3 H < a_T \beta_3 H$ and $\theta K_T H < b_T + \beta_3 H$, in other words if grouse death rate is higher than grouse birth rates, if tick birth rate is higher than tick death rate and transmission on the non-viraemic host cannot occur, i.e. ticks are lost more quickly than they transmit infection.

3) At $(K_g, 0, 0, 0, 0)$ the eigenvalues of the Jacobian are given by the following:

$$\begin{vmatrix} -r_g - \lambda & a_g - 2r_g & a_g - 2r_g & 0 & -\beta_1 K_g \\ 0 & -\Gamma - \lambda & 0 & 0 & \beta_1 K_g \\ 0 & \gamma & -b_g - \lambda & 0 & 0 \\ 0 & 0 & 0 & a_T \beta_3 H - b_T - \beta_3 H - \lambda & a_T \beta_3 H \\ 0 & 0 & 0 & 0 & -b_T - \beta_3 H - \lambda \end{vmatrix} = 0$$

The solutions of this are $\lambda = -r_g, -b_T - \beta_3 H, -\Gamma, -b_g$ and $a_T \beta_3 H - b_T - \beta_3 H$. Clearly the eigenvalues are negative iff $r_g > 0$ and $a_T \beta_3 H < b_T + \beta_3 H$ i.e. grouse reproductive rate is positive and tick reproductive rate is negative.

4) At $(K_g, 0, 0, K_T, 0)$ the eigenvalues of the Jacobian are given by the following

$$\begin{vmatrix} -r_g - \lambda & a_g - 2r_g & a_g - 2r_g & 0 & -\beta_1 K_g \\ 0 & -\Gamma - \lambda & 0 & 0 & \beta_1 K_g \\ 0 & \gamma & -b_g - \lambda & 0 & 0 \\ 0 & -\beta_2 K_T & 0 & s_T K_T \beta_3 H - \lambda & a_T \beta_3 H - 2s_T K_T \beta_3 H - \theta K_T H \\ 0 & \beta_2 K_T & 0 & 0 & \theta K_T H - b_T - \beta_3 H - \lambda \end{vmatrix} = 0$$

The solutions of this are $\lambda = -r_g, -s_T K_T \beta_3 H, -b_g$ and the solutions of

$$\begin{vmatrix} -\Gamma - \lambda & \beta_1 K_g \\ \beta_2 K_T & \theta K_T H - b_T - \beta_3 H - \lambda \end{vmatrix} = 0$$

The first three solutions are negative as long as $r_g > 0$ and $a_T \beta_3 H > b_T + \beta_3 H$. The determinant gives the following quadratic

$$\lambda^2 + \lambda(\Gamma + b_T + \beta_3 H - \theta K_T H) - \beta_1 \beta_2 K_g K_T - \Gamma(\theta K_T H - b_T - \beta_3 H) = 0$$

which has roots with negative real parts iff $\Gamma(b_T + \beta_3 H) > \theta K_T H \Gamma + \beta_1 \beta_2 K_g K_T$ i.e. if $R_{0,virus} < 1$.

5) At $(0, 0, 0, T_s^+, T_i^+)$ the eigenvalues of the Jacobian are given by

$$\begin{vmatrix} r_g - \beta_1 T_i^+ - \lambda & a_g & a_g & 0 & 0 \\ \beta_1 T_i^+ & -\Gamma - \lambda & 0 & 0 & 0 \\ 0 & \gamma & -b_g - \lambda & 0 & 0 \\ 0 & -\beta_2 T_s^+ & 0 & -s_T K_T \beta_3 H - \theta T_i^+ H - \lambda & a_T \beta_3 H - 2s_T K_T \beta_3 H - \theta T_s^+ H \\ 0 & \beta_2 T_s^+ & 0 & \theta T_i^+ H & \theta T_s^+ H - b_T - \beta_3 H - \lambda \end{vmatrix} = 0.$$

This can be split into two independent determinants

$$\begin{vmatrix} r_g - \beta_1 T_i^+ - \lambda & a_g & a_g \\ \beta_1 T_i^+ & -\Gamma - \lambda & 0 \\ 0 & \gamma & -b_g - \lambda \end{vmatrix} = 0$$

and

$$\begin{vmatrix} -s_T K_T \beta_3 H - \theta T_i^+ H - \lambda & a_T \beta_3 H - 2s_T K_T \beta_3 H - \theta T_s^+ H \\ \theta T_i^+ H & \theta T_s^+ H - b_T - \beta_3 H - \lambda \end{vmatrix} = 0.$$

Considering the first determinant we get the following cubic.

$$\lambda^3 + \lambda^2(\Gamma + b_g + \beta_1 T_i^+ - r_g) + \lambda(\Gamma b_g - \beta_1 T_i^+ r_g + \beta_1 T_i^+ \Gamma - r_g(\Gamma + b_g)) - r_g b_g \Gamma + \beta_1 T_i^+ \alpha b_g - \beta_1 T_i^+ r_g b_g - \beta_1 T_i^+ r_g \gamma = 0$$

In order to see when this cubic has roots with negative real parts we check the Routh Hurwitz conditions which say that if we have a cubic of the form

$$\lambda^3 + A\lambda^2 + B\lambda + C = 0$$

Then the roots have negative real parts iff $A, B, C > 0$ and $AB > C$. In this case, we can see that these conditions hold if $a_g < b_g$ i.e. if $r_g < 0$. If we consider the second determinant we get the following quadratic:

$$\lambda^2 + \lambda(s_T K_T \beta_3 H + \theta T_i^+ H) - \theta T_i^+ H(a_T \beta_3 H - 2s_T K_T \beta_3 H - \theta T_s^+ H) = 0$$

In the case of a quadratic of the form

$$\lambda^2 + A\lambda + B = 0$$

The Routh Hurwitz conditions say that the roots have negative real parts iff $A > 0$ and $B > 0$. In this case $A > 0$ iff $K_T > 0$ and $T_i^+ > 0$ and $B > 0$ iff $b_T + \beta_3 H < a_T \beta_3 H$. Therefore for stability and biological relevance of this equilibrium we need $b_T + \beta_3 H < a_T \beta_3 H$ and $\theta K_T H > b_T + \beta_3 H$ and $a_g < b_g$.

6) Due to the complexity of the algebraic analysis in this case, the coexistence equilibrium in which grouse and ticks persist with the virus is assumed to be the stable equilibrium (or replaced with stable limit cycles) when none of the other equilibria are stable. Numerical simulations back up this assumption.

References

- Beasley, S.J., Campbell, J.A., Reid, H.W.: Threshold problems in infection of *Ixodes ricinus* with the virus of Louping ill. Tick borne disease and their vectors. Proceedings of an international conference held in Edinburgh from 27th September to 1st October 1976. Edited by J.K.H Wilde (1978)
- Cooksey, L.M., Haile, D.G., Mount, G.A.: Computer simulation of Rocky Mountain Spotted fever transmission by the American dog tick (Acari:ixodidae). *J. Med. Ent.* **27**(4), 671–680 (1990)
- Hudson, P.J.: Red Grouse: the biology and management of a wild gamebird. The report of the North of England Grouse Research Project 1977–1985, Game Conservancy Trust, Fordingbridge (1986)
- Hudson, P.J.: Grouse in space and time: the population biology of a managed gamebird. The report of the Game conservancy's Scottish Grouse Research project and North of England Grouse Research project. Game Conservancy Trust Fordingbridge (1992)
- Hudson, P.J., Norman, R., Laurenson, M.K., Newborn, D., Gaunt, M., Jones, L., Reid, H., Gould, E., Bowers, R., Dobson, A.: Persistence and transmission of tick-borne viruses: *Ixodes ricinus* and louping-ill virus in red grouse populations. *Parasitology* **111**, 549–558 (1995)

- Jenkins, D., Watson, A., Miller, G.R.: Population fluctuations in the red grouse *Lagopus lagopus scoticus*. *J. Anim. Ecol.* **36**, 97–122 (1967)
- Jones, L.D., Davies, C., Steele, G.M., Nuttall, P.A.: A novel mode of arbovirus transmission involving a non-viraemic host. *Science* **237**, 775–777 (1987)
- Jones, L.D., Davies, C.R., Williams, T., Cory, J., Nuttall, P.A.: Non-viraemic transmission of Thogoto virus- vector efficiency of *Rhipicephalus appendiculatus* and *Amblyomma variegatum*. *Trans. Roy.Soc Trop.Med. Hyg.* **84**(6), 846–848 (1990)
- Jones, L.D., Kaufman, W.R., Nuttall, P.A.: Modification of the skin feeding site by tick saliva mediates virus transmission. *Experientia* **48**(8), 779–782 (1992)
- Jones, L.D., Gaunt, M., Hails, R.S., Laurenson, K., Hudson, P.J., Reid, H., Henbest, P., Gould, E.A.: Efficient transfer of Louping ill virus between infected and uninfected ticks co-feeding on mountain hares (*Lepus timidus*). *Med. Vet. Entomol.* **142**(6), 1181–1191 (1997)
- Labuda, M., Jones, L.D., Williams, T., Nuttall, P.A.: Enhancement of tick-borne encephalitis transmission by tick salivary gland extracts. *Med. Vet. Entomol.* **7**(2), 193–196 (1993a)
- Labuda, M., Nuttall, P.A., Kozuch, O., Eleckova, E., Williams, T., Zuffova, E., Sabo, A.: Non-viraemic transmission of tick-borne encephalitis virus: a mechanism for arbovirus survival in nature. *Experientia* **49**, 802–805 (1993b)
- Norman, R., Bowers, R.G., Begon, M., Hudson, P.J.: Persistence of tick borne virus in the presence of multiple host species: ticks act as reservoirs and result in parasite mediated competition. *J. Theor. Biol.* **200**, 111–118 (1999)
- O'Callaghan, C.J., Medley, G.F., Peter, T.F., Perry, B.D.: Investigating the epidemiology of heartwater (*Cowdria ruminantium* infection) by means of a transmission dynamics model. *Parasitology* **117**, 49–61 (1998)
- Ogden, N.H., Nuttall, P.A., Randolph, S.E.: Natural Lyme disease cycles maintained via sheep by cofeeding ticks. *Parasitology* **115**(6), 591–599 (1997)
- Randolph, S.E., Gern, L., Nuttall, P.A.: Co-feeding ticks, Epidemiological significance for tick-borne pathogen transmission. *Parasitology Today* **12**(12), 472–479 (1996)
- Reid, H.W.: Experimental infection of red grouse with Louping ill virus (flavivirus group) I. The viraemia and antibody response. *J. Comp. Path.* **85**, 223–229 (1975)
- Reid, H.W.: The epidemiology of Louping ill. In: Wilde, J.K.H. (ed.), *Tick Borne Disease and their Vectors*. Proceedings of an International Conference held in Edinburgh 27th September to 1st October 1976 (1978)
- Sonenshine, D.E., Mather T.N.: *Ecological dynamics of tick-borne zoonoses*. O.U.P New York (1994)