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Disease propagation in connected host populations with density-dependent dynamics: the case of the Feline Leukemia Virus

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Abstract

Spatial heterogeneity is a strong determinant of host-parasite relationships, however local-scale mechanisms are often not elucidated. Generally speaking, in many circumstances dispersal is expected to increase disease persistence. We consider the case when host populations show density-dependent dynamics and are connected through the dispersal of individuals. Taking the domestic cats *(Felis catus)*—Feline Leukemia Virus (FeLV) as a toy model of host-microparasite system, we predict the disease dynamics when two host populations with distinct or similar structures are connected together and to the surrounding environment by dispersal. Our model brings qualitatively different predictions from one-population models. First, as expected, biologically realistic rates of dispersal may allow FeLV to persist in sets of populations where the virus would have gone extinct otherwise, but a reverse outcome is also possible: eradication of FeLV from a small population by connexion to a larger population where it is not persistent. Second, overall prevalence as well as depression of host population size due to infection are both enhanced by dispersal, even at low dispersal rates when disease persistence is not achieved in the two populations. This unexpected prediction is probably due to the combination of dispersal with density-dependent population dynamics. Third, the dispersal of non-infectious cats has more influence on virus prevalence than the dispersal of infectious. Finally, prevalence and depression of host population size are both related to the rate of dispersion, to the health status of individuals dispersing and to the dynamics of host populations.

Keywords: Density-dependence; Dispersal; Epidermiology model; Feline leukemia virus; *Felis catus*; Spatial heterogeneity

1. Introduction

The metapopulation concept constitutes a fruitful approach to study the influence of spatial heterogeneity on the dynamics of host-parasite systems (Grenfell and Harwood, 1997). Generally speaking, spatial heterogeneity is thought to have a stabilizing effect on host-parasite systems (Pimentel et al., 1963). Specifically, it can increase disease persistence (Post et al., 1983; Wood and Thomas, 1996), reduce the occurrence of fade-outs (Hassell et al., 1991 in parasitoids) and drive epidemic cycles (Bolker and Grenfell, 1995). The influence of parasites on host demography also depends on spatial structure (Hess, 1994; Gog et al., 2002; McCallum and Dobson, 2002). Spatial heterogeneity is supposed to act through phase differences between oscillations in patches: if patches become synchronized then spatial effects disappear. For this reason several authors addressed the dynamics of patch coupling (Lloyd and May, 1996; Earn et al., 1998; Swinton et al., 1998).

Our starting point is to study how host dispersal among populations of domestic cat (*Felis catus*) affects the dynamics of Feline Leukemia Virus (FeLV). Previous non-spatially designed models predicted that FeLV dynamics depends on the size of the host population under consideration and on the relationship between host density and the pattern of contacts (Fromont et al., 1998b). This distinction was made in accordance with previous data (Fromont et al., 1998a). However, in a rural environment, cat populations are connected to each other through dispersal (Liberg, 1980). Our aim is to test whether dispersal has any influence on FeLV propagation.

Several formulations have been introduced to model spatial dynamics of epidemics (Faddy, 1986; Lloyd and May, 1996). In order to choose an appropriate form for the model we assess how hosts use space at the scale considered (Hastings, 1990). We consider domestic cats

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living with human beings in villages separated from each other (Fromont et al., 1998a). A cat population is defined by all cats living in a village or a farm and contacts between cats from different villages occur through dispersal. We thus represent space in a discretized way—i.e., n populations are connected to each other—thus we may use either patch-coupling models (Hassell et al., 1991) or lattice models considering space as a grid of cells, each cell including a population (Durrett, 1995). Lattice models represent systems where numerous cells are connected (White et al., 1995). Here, because we intend to detail the local dynamics of the system and its biological relevance, we use patch coupling. We derive a model with n populations but analyse the case when $n = 2$, as the minimal model to investigate the influence of dispersal rate and of the characteristics of dispersers.

Within local host populations, the density and spatial distribution of hosts also influence the rate of contacts among individuals, and thus the incidence of diseases (Blower and Roughgarden, 1989; Diekmann et al., 1995; McCallum et al., 2001). In the case of FeLV, models designed for large populations assumed frequency-dependent incidence and predicted no threshold population size for virus persistence, whereas models of small populations assumed density-dependent transmission and predicted the possibility of FeLV extinction (Fromont et al., 1998b). For this reason, and contrarily to many previous models (Post et al., 1983; Jansen and Lloyd, 2000; Keeling and Rohani, 2002), we assume density-dependent host population dynamics (Begon et al., 1992) and frequency-dependent or density-dependent incidence depending on population size.

Finally, in discrete-space models, two modes of disease propagation can be distinguished: contact and dispersal. In contact models, individuals from one population directly infect individuals from other populations or temporarily migrate to another population (Keeling and Rohani, 2002), for example during the reproduction period. However, in cat populations, dispersal is definitive: males disperse from their native home range under the pressure of dominant males and settle in areas where no dominant male is established. When a resident male dies, his home range is soon occupied by a new, usually immigrating, male (Liberg, 1980). The relevant process is thus dispersal (Bailey, 1975), contrarily to assumption made by numerous previous models (Nold, 1980; Post et al., 1983; May and Anderson, 1984; Hethcote and Van Ark, 1987; Andreasen and Christiansen, 1989; Swinton et al., 1998). We also test the influence of the characteristics of dispersers on FeLV dynamics. In a rural environment, dispersal mainly concerns more than 2 years old, sexually mature males. Because young adult males are among the categories most often infected by FeLV (Fromont et al., 1998a), we investigate whether dispersal of infectious cats has the same influence than dispersal of non-infectious ones.

We thus propose a model including two hypotheses that are not usually considered in spatial epidemiological models: density-dependent host population dynamics and host dispersal. Our aim is to apply such hypotheses to the case of FeLV-cat system where they are biologically relevant. We examine the predictions of the model in terms of disease persistence, prevalence and influence on host population dynamics.

2. Materials and methods

2.1. Host population structure and growth

The typical structure of the environment modelled here is a set of discrete villages and farms in an agricultural landscape. We consider n host populations, each of them living on a specific patch (either farm or village) and having there its own dynamics. In order to take into account other, non-specified populations surrounding the studied populations we consider a population of cats, called matrix, whose dynamics is mostly unaffected by the n populations (Fig. 1); the matrix could represent transient feral males of unknown origin that are recorded at all times of the year around cat populations (Liberg, 1980), some of them being cats dispersing from unknown populations.

The model deals with numbers of individuals, as opposed to densities (however, in a given population,

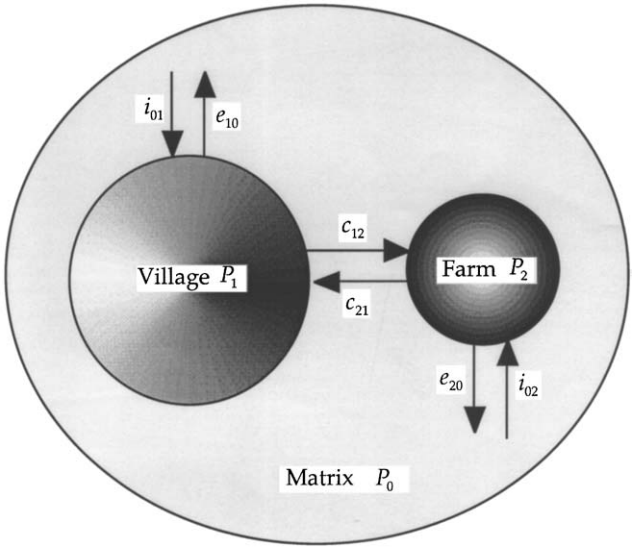

Fig. 1. Typical structure and dispersal rates in a system considered in the model. Several populations (here, one village and one farm) are connected to each other by exchange rates c_{ij}. The matrix represents transient feral males of unknown origin. Cats emigrate from each population to the matrix at rate e_{i0} and immigrate from the matrix to each population at rate i_{0i}.

field observations suggest that the spatial range occupied by the population does not change when the number of cats changes, thus density and numbers are highly correlated). The dynamics of cat populations has been described previously (Fromont et al., 1998b). In our model, $P_i = P_i(t) \geqslant 0$ equals the total number of cats at time t in the ith population ($1 \leqslant i \leqslant n$). Let $\beta_i(P_i) \geqslant 0$ and $\delta_i(P_i) \geqslant 0$ be the fertility and mortality functions, respectively. Let $g_i(P_i) = \beta_i(P_i) - \delta_i(P_i)$, be the intrinsic growth rate of the ith population. When a population is free from FeLV and isolated, its dynamics is governed by the ordinary differential equation

$$P_i' = (\beta_i(P_i) - \delta_i(P_i))P_i, \quad t \geqslant 0. \tag{1}$$

Here we consider populations showing logistic-type growth, namely $\beta_i(P_i)$ is a constant birth rate $b_i > 0$, independent of population size, and $\delta_i(P_i)$ is a density-dependent mortality function: $\delta_i(P_i) = m_i + (r_i/K_i)P_i$, $r_i = b_i - m_i > 0$, $m_i > 0$, where m_i is the natural death rate. K_i is the unique positive stationary solution of (1), globally asymptotically stable for $P_i(0) > 0$. K_i is the carrying capacity of the environment on the ith patch.

The within-population model also takes into account some features of host population structure by using different incidence functions. Cat populations show variable density, from 1 cat/km^2 in places where food resources are scarce to 2000 cats/km^2 around abundant, clumped food resources. Spatial and social structures of cat populations vary with density (Liberg et al., 2000). As a consequence, we proposed a qualitative relationship between host density and contact rate, leading to different incidence functions according to the population considered (Fromont et al., 1998b). Here we are interested in cats living at intermediate density (10–100 cats/km^2) in the rural environment. Small populations, i.e., places where carrying capacities lies under 50 cats, are designated as "farms" and have a density-dependent transmission (De Leo and Dobson, 1996), otherwise called "mass action" (Anderson and May, 1979) or "pseudo mass action" (De Jong et al., 1995), because all cats in a population are expected to encounter each other. On the contrary, in populations where carrying capacity stands above 60 individuals, thereafter called "villages", an individual only has contact with its neighbours and homogeneous mixing cannot be assumed. In villages, we use frequency-dependent incidence (De Leo and Dobson, 1996), originally named "proportionate mixing" (Hethcote and Yorke, 1984) or "true mass action" (De Jong et al., 1995).

3. FeLV transmission within a single isolated population

The clinical course of FeLV has been described previously (Hoover and Mullins, 1991; Hardy, 1993). In the ith population, we denote $X_i = X_i(t)$, $Y_i = Y_i(t)$ and $Z_i = Z_i(t)$ the respective numbers of susceptible, infectious (or viremic) and immune individuals, so that $P_i = X_i + Y_i + Z_i$ represents the total population. Note that infectious and immunes are not defined as in SIR classical models. Here infected individuals become either infectious or immune, and then stay in their class lifelong (Charreyre and Pedersen, 1991; Hoover and Mullins, 1991). Let $\sigma_i(X_i, Y_i, Z_i)$ be the incidence function, i.e. the number of newly infected cats per unit of time and let π_i, $0 \leqslant \pi_i \leqslant 1$, be the proportion of infected cats developing FeLV viremia. Lastly $\alpha_i > 0$ is the additional mortality rate of infectious cats due to FeLV.

When the ith population is isolated, the dynamics of the propagation of FeLV within this population is governed by a set of three ordinary differential equations:

$$\begin{cases} X_i' = -\sigma_i(X_i, Y_i, Z_i) & +b_i(X_i + Z_i) & -\delta_i(P_i)X_i, \\ Y_i' = \pi_i\sigma_i(X_i, Y_i, Z_i) & -\alpha_i Y_i & -\delta_i(P_i)Y_i, \\ Z_i' = (1 - \pi_i)\sigma_i(X_i, Y_i, Z_i) & & -\delta_i(P_i)Z_i \end{cases} \tag{2}$$

together with the initial conditions $X_i(0) > 0$, $Y_i(0) > 0$, $Z_i(0) \geqslant 0$. The ordinary differential equation for the total population reads $P_i' = [b_i - \delta_i(P_i^*)]P_i^* - (\alpha_i + b_i)Y_i$. The incidence function takes one of the two forms: $\sigma_i(X_i, Y_i, Z_i) = \sigma_{i,ma}X_iY_i$, $\sigma_{i,ma} > 0$ for density-dependent transmission or $\sigma_i(X_i, Y_i, Z_i) = \sigma_{i,pm}(X_iY_i/P_i)$, $\sigma_{i,pm} > 0$ for frequency-dependent transmission.

Assuming that this ith population is isolated from others, including the matrix, the reproductive number $R_{i,0}$ is given by (Fromont et al., 1997, 1998b)

$$R_{i,0}^{ma} = \frac{\pi_i\sigma_{i,ma}K_i}{b_i + \alpha_i},$$
$$R_{i,0}^{pm} = \frac{\pi_i\sigma_{i,pm}}{b_i + \alpha_i}$$

for the density-dependent and frequency-dependent transmission, respectively. FeLV will not develop in this isolated population, i.e. the stationary state $(K_i, 0, 0)$ of (2) is locally asymptotically stable (LAS), when $R_{i,0} \leqslant 1$. As a consequence there is no threshold population level in the frequency-dependent model, but there is one in the density-dependent model, as classically described (McCallum et al., 2001).

4. Dispersal among populations

In the matrix we denote $X_0 = X_0(t)$, $Y_0 = Y_0(t)$ and $Z_0 = Z_0(t)$ the respective numbers of susceptible, infectious and immune individuals, so that $P_0 = X_0 + Y_0 + Z_0$ represents its total population. These are not considered dynamical variables but they are assumed to be constant in time (see hypotheses (H0), (H1) and (H5)

below). We distinguish three types of dispersal among populations (Fig. 1):

- Dispersal from the matrix, i.e. population P_0, to any of the n populations is called "immigration"; the immigration rates from the matrix to population i are i_{0i}^X in the susceptible class, i_{0i}^Y in the infectious class and i_{0i}^Z in the immune class.
- Dispersal from any of the n populations to the matrix is called "emigration"; the emigration rates from population i to the matrix are e_{i0}^X in the susceptible class, e_{i0}^Y in the infectious class and e_{i0}^Z in the immune class.
- Dispersal between any two of the n populations is called "exchange"; the exchange rates from population i to population j are c_{ij}^X in the susceptible class, c_{ij}^Y in the infectious class and c_{ij}^Z in the immune class.

For the sake of simplicity, we neglect mortality during dispersal and we consider that cats entering in a new population behave like native individuals, particularly concerning their rate of contact with other individuals. Our full model with n populations reads:

$$\begin{aligned}
X_i' &= -\sigma_i(X_i, Y_i, Z_i) + b_i(X_i + Z_i) \\
&\quad - \delta_i(P_i)X_i - \sum_{j\neq i} c_{ij}^X X_i \\
&\quad + \sum_{j\neq i} c_{ji}^X X_j - e_{i0}^X X_i + i_{0i}^X X_0, \\
Y_i' &= \pi_i\sigma_i(X_i, Y_i, Z_i) - \alpha_i Y_i - \delta_i(P_i)Y \\
&\quad - \sum_{j\neq i} c_{ij}^Y Y_i + \sum_{j\neq i} c_{ji}^Y Y_j - e_{i0}^Y Y_i - \sum_{j\neq i} c_{ij}^Z Z_i + i_{0i}^Y Y_0, \\
Z_i' &= (1-\pi_i)\sigma_i(X_i, Y_i, Z_i) - \delta_i(P_i)Z_i \\
&\quad - \sum_{j\neq i} c_{ij}^Z Z_i + \sum_{j\neq i} c_{ji}^Z Z_j - e_{i0}^Z Z_i + i_{0i}^Z Z_0.
\end{aligned}$$

We analyse the model regarding the persistence of viremia, the prevalence (frequency) of viremia and the depression of host population size due to infection. Depression is defined as the difference between host population size with and without virus (in percent of population size without virus).

5. Results

The dynamics of the propagation of FeLV through n populations and a matrix is governed by a set of $3n$ ordinary differential equations. We analyse here this dynamics when $n = 2$ populations are connected, placing various assumptions on local population structures, on the epidemiological status of the matrix, and on the rates of exchange, emigration and immigration. Our two populations model reads:

$$\begin{aligned}
X_1' &= -\sigma_1(X_1, Y_1, Z_1) + b_1(X_1 + Z_1) \\
&\quad - \delta_1(P_1)X_1 - (c_{12}^X + e_{10}^X)X_1 + c_{21}^X X_2 + i_{01}^X X_0, \\
Y_1' &= \pi_1\sigma_1(X_1, Y_1, Z_1) - \alpha_1 Y_1 - \delta_1(P_1)Y_1 \\
&\quad - (c_{12}^Y + e_{10}^Y)Y_1 + c_{21}^Y Y_2 + i_{01}^Y Y_0, \\
Z_1' &= (1-\pi_1)\sigma_1(X_1, Y_1, Z_1) - \delta_1(P_1)Z_1 \\
&\quad - (c_{12}^Z + e_{10}^Z)Z_1 + c_{21}^Z Z_2 + i_{01}^Z Z_0, \\
X_2' &= -\sigma_2(X_2, Y_2, Z_2) + b_2(X_2 + Z_2) \\
&\quad - \delta_2(P_2)X_2 - (c_{21}^X + e_{20}^X)X_2 + c_{12}^X X_1 + i_{02}^X X_0, \\
Y_2' &= \pi_2\sigma_2(X_2, Y_2, Z_2) - \alpha_2 Y_2 \\
&\quad - \delta_2(P_2)Y_2 - (c_{21}^Y + e_{20}^Y)Y_2 + c_{12}^Y Y_1 + i_{02}^Y Y_0, \\
Z_2' &= (1-\pi_2)\sigma_2(X_2, Y_2, Z_2) - \delta_2(P_2)Z_2 \\
&\quad - (c_{21}^Z + e_{20}^Z)Z_2 + c_{12}^Z Z_1 + i_{02}^Z Z_0
\end{aligned} \tag{3}$$

together with the set of initial conditions $X_i(0)\geqslant 0$, $Y_i(0) > 0$, $Z_i(0)\geqslant 0$, $i = 1, 2$.

5.1. Population dynamics in the absence of virus

We first analyse the model with no infectious and no immune cat in any population. In this setting the dynamics of the interactions between the two populations is governed by a system of two ordinary differential equations:

$$\begin{aligned}
P_1' &= (b_1 - \delta_1(P_1))P_1 - (c_{12}^X + e_{10}^X)P_1 + c_{21}^X P_2 + i_{01}^X P_0, \\
P_2' &= (b_2 - \delta_2(P_2))P_2 - (c_{21}^X + e_{20}^X)P_2 + c_{12}^X P_1 + i_{02}^X P_0
\end{aligned} \tag{4}$$

together with the initial data $P_1(0)\geqslant 0$, $P_2(0)\geqslant 0$; we write P_0 instead of X_0.

A stationary state for (4) is a couple (P_1^*, P_2^*) with $0\leqslant P_1^*, P_2^*$, solution of the nonlinear system

$$\begin{aligned}
0 &= (b_1 - \delta_1(P_1))P_1^* - (c_{12}^X + e_{10}^X)P_1^* + c_{21}^X P_2^* + i_{01}^X P_0, \\
0 &= (b_2 - \delta_2(P_2))P_2^* - (c_{21}^X + e_{20}^X)P_2^* + c_{12}^X P_1^* + i_{02}^X P_0.
\end{aligned} \tag{5}$$

By direct substitution in (5), the trivial stationary state (0, 0), corresponding to the extinction of both populations is feasible if and only if

(H1) $\quad i_{01}^X P_0 = i_{02}^X P_0 = 0,$

i.e., if and only if there is no immigration from the matrix towards the two populations. Then, still assuming (H1) satisfied, (0,0) is LAS, i.e. both populations go extinct, if the following set of linear inequalities in the variables c_{12}^X and c_{21}^X holds:

$$\text{(C1)} \quad \begin{cases} r_1 - e_{10}^X - c_{12}^X \leqslant 0, & \text{(C1.1)} \\ r_2 - e_{20}^X - c_{21}^X \leqslant 0, & \text{(C1.2)} \\ (r_1 - e_{10}^X - c_{12}^X)(r_2 - e_{20}^X - c_{21}^X) - c_{12}^X c_{21}^X \geqslant 0, & \text{(C1.3)} \end{cases}$$

in which case it is globally asymptotically stable (GAS). The stability condition (C1) can be represented using a graphical representation in the variables $r_i - e_{i0}^X - c_{ij}^X$ (Fig. 2); $r_i - e_{i0}^X - c_{ij}^X$ represents the intrinsic population

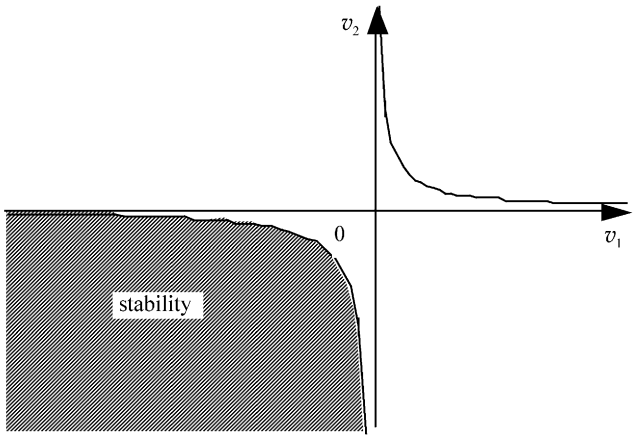

Fig. 2. The shaded area represents the two-dimensional zone delimited by the set of inequalities $v_1 \leqslant 0$, $v_2 \leqslant 0$, $v_1 v_2 - c \geqslant 0$ when $c \geqslant 0$. It is used in the text to depict condition (C1) for $v_1 = r_1 - e_{10}^X - c_{12}^X$, $v_2 = r_2 - e_{20}^X - c_{21}^X$, $c = c_{21}^X c_{12}^X$ and condition (C2) for $v_1 = A_1 - e_{10}^Y - c_{12}^Y$, $v_2 = A_2 - e_{20}^Y - c_{21}^Y$, $c = c_{21}^Y c_{12}^Y$.

growth rate of population i minus the emigration rate from population i towards the matrix and population j. In the following, "net growth rate" of population i will stand for $r_i - e_{i0}^X - c_{ij}^X$. Stability and unstability zones depend on the signs of net growth rates: when at least one population has a positive net growth rate then (0, 0) is unstable, i.e., at least one population does not go extinct. When both net growth rates are nonpositive then (0, 0) is stable provided c_{12}^X and c_{21}^X be small enough; as an example, this is the case when either $c_{12}^X = 0$ or $c_{21}^X = 0$, this is, when there is no exchange from one population to the other one.

A semi-trivial stationary state $(0, P_2^*), P_2^* > 0$ corresponding to the extinction of the first population and persistence of the second one is feasible if and only if

$$\text{(H2)} \quad i_{01}^X P_0 = 0, \;\; c_{21}^X = 0 \quad \text{and either } r_2 - e_{20}^X > 0 \text{ or } i_{02}^X P_0 > 0,$$

i.e., if and only if there is no immigration of individuals from the matrix or from population 2 towards population 1, and either a positive net growth rate for population 2 or a positive immigration from the matrix to population 2. Then, still assuming (H2) holds, $(0, P_2^*)$ is GAS provided (C1.1) holds.

A similar analysis works for a semi-trivial state $(P_1^*, 0), P_1^* > 0$: a unique one exists if and only if

$$\text{(H3)} \quad i_{02}^X P_0 = 0, \;\; c_{12}^X = 0 \quad \text{and either } r_1 - e_{10}^X > 0 \text{ or } i_{01}^X P_0^* > 0$$

and, still assuming (H3) to hold it is GAS provided (C1.2) holds.

We are left with looking for a stationary state $(P_1^*, P_2^*), P_1^* > 0, P_2^* > 0$ corresponding to the coexistence of both populations. A unique such a stationary state exists in four situations, namely when:

- (H2) holds, but (C1.1) is not satisfied, say $r_1 - e_{10}^X > c_{12}^X$;
- (H3) holds, but (C1.2) is not satisfied, say $r_2 - e_{20}^X > c_{21}^X$;
- (H4) $i_{01}^X P_0 > 0, i_{02}^X P_0 > 0$;
- (H1) holds, (C1.1) and (C1.2) hold, but (C1.3) is not satisfied.

Fig. 3 provides an alternative description of these conditions. Last, assuming either one of these four conditions to hold, then this unique positive stationary state is GAS.

Finally, for latter purposes it is necessary to compare any existing persistent state (P_1^*, P_2^*) to the corresponding carrying capacities (K_1, K_2). Toward this end set $P_i^* = K_i + u_i$, $i = 1, 2$. Note that $-K_i < u_i < 0 \rightleftharpoons [b_i - \delta_i(P_i^*)]P_i^* > 0$, $i = 1, 2$. Then, adding the two equations in (5) yields

$$[b_1 - \delta_1(P_1^*)]P_1^* + [b_2 - \delta_2(P_2^*)]P_2^* + (i_{01}^X + i_{02}^X)P_0^* - (e_{10}^X K_1 + e_{20}^X K_2) = e_{10}^X u_1 + e_{20}^X u_2. \quad (6)$$

The quantity $(i_{01}^X + i_{02}^X)P_0^* - (e_{10}^X K_1 + e_{20}^X K_2)$ is the balance of emigration versus immigration between the two populations and the matrix. When it is positive at least one population settles above its carrying capacity, when it is negative at least one settles below its carrying capacity and when it is 0 one settles above and the other one settles below. When exchange, emigration and immigration rates go to 0 then a continuity argument shows that $(P_1^*, P_2^*) \to (K_1, K_2)$.

5.2. FeLV propagation in two populations with disease-free matrix

In this part we analyse which conditions allow for the persistence of disease in two connected populations. We

	$i_{01}^X P_0 = 0$, $i_{02}^X P_0 = 0$	$i_{01}^X P_0 = 0$, $i_{02}^X P_0 > 0$	$i_{01}^X P_0 > 0$, $i_{02}^X P_0 = 0$	$i_{01}^X P_0 > 0$, $i_{02}^X P_0 > 0$
$(0, 0)$	(C1.1), (C1.2) & (C1.3)	--	--	--
$(0, P_2^\star)$	(C1.1), $c_{21}^X = 0$ & non-(C1.2)	(C1.1) & $c_{21}^X = 0$	--	--
$(P_1^\star, 0)$	(C1.2), $c_{12}^X = 0$ & non-(C1.1)	--	(C1.2) & $c_{12}^X = 0$	--
$(P_1^\star, P_2^\star)$	(C1.1), (C1.2), non-(C1.3); non-(C1.1), $c_{12}^X = 0$; non-(C1.2), $c_{21}^X = 0$; non-(C1.1), non-(C1.2).	either $c_{21}^X = 0$ or non-(C1.1)	either $c_{12}^X = 0$ or non-(C1.2)	G.A.S.

Fig. 3. Existence and global stability conditions for stationary states of (4). If condition (C) is $\alpha \leqslant \beta$ then condition non-(C) is $\alpha > \beta$; also -- means non-feasible. Note that when (H1) is satisfied (left column), then four different set of conditions lead to the existence and stability of a persistent state.

first assume that there is no immigration of infectious or immune individuals from the matrix and that the number of susceptible individuals in the matrix is a constant, say

(H5) $X_0(t) = P_0 \geqslant 0, i_{oi}^Y Y_0(t) = i_{oi}^Z Z_0(t) = 0.$

This also contains the model with no infectious in the matrix. The dynamics of the propagation of FeLV is governed by (3), assuming (H5) satisfied. Let us assume:

(H6) in the absence of virus,

there is a unique persistent state (P_1^*, P_2^*)

(see above or Fig. 3 for details). Then the disease free state $(P_1^*0, 0, P_2^*, 0, 0)$ is a stationary state if and only if there is no immigration of infectious or immune individuals from the matrix, which is actually the case from hypothesis (H5) (this is seen by direct substitution in (3)). Analysing the local stability of $(P_1^*0, 0, P_2^*, 0, 0)$ will tell us whether FeLV can develop when there is no supply of infectious or immune individuals from the matrix. Toward this end, let us introduce for the ith population a parameter A_i defined as

$$A_i = \begin{cases} \pi_i \sigma_{i,ma} P_i^* - (\delta_i(P_i^*) + \alpha_i) \text{ density-dependent transmission,} \\ \pi_i \sigma_{i,pm} - (\delta_i(P_i^*) + \alpha_i) \text{ frquency-dependent transmission,} \end{cases}$$

A_i is to be interpreted as the intrinsic growth rate of the infectious class in the ith population $i = 1, 2$ at equilibrium when emigration and exchange are neglected in this very class. Then, assuming condition (H5) is satisfied, $(P_1^*, 0, 0, P_2^*, 0, 0)$ is LAS if the following set of inequalities in the variables c_{12}^Y, e_{10}^Y, c_{21}^Y and e_{20}^Y holds:

$$\text{(C2)} \quad \begin{cases} A_1 - e_{10}^Y - c_{12}^Y \leqslant 0, & \text{(C2.1)} \\ A_2 - e_{20}^Y - c_{21}^Y \leqslant 0, & \text{(C2.2)} \\ (A_1 - e_{10}^Y - c_{12}^Y)(A_2 - e_{20}^Y - c_{21}^Y) - c_{21}^Y c_{12}^Y \geqslant 0. & \text{(C2.3)} \end{cases}$$

Condition (C2) can be represented by using a graphical representation in the variables $A_i - e_{i0}^Y - c_{ij}^Y$ (Fig. 2). Fig. 2 shows that (C2) is similar to (C1), but concerning the infectious class only. Again, stability zones depend on the signs of $A_i - e_{i0}^Y - c_{ij}^Y$ which can be interpreted as the " net growth rate of the infectious class in the ith population": when at least one net growth rate of infectious class is positive then $(P_1^*0, 0, P_2^*, 0, 0)$ is unstable, while when both are nonpositive then $(P_1^*0, 0, P_2^*, 0, 0)$ is LAS provided both c_{ij}^Y be small enough.

For small emigration rates e_{i0}^Y, $i = 1, 2$ in infectious classes with respect to A_i, the stability condition (C2) relies on the signs of A_1 and A_2 which, in turn, depend on the rates of exchange and emigration of susceptible individuals through P_1^* and P_2^*. Once these are prescribed, and for small emigration rates in infectious classes, the stability analysis relies on the exchange rates for infectious individuals, no role being played by immune individuals. Using $u_i = P_i^* - K_i$ introduced earlier and the reproductive numbers $R_{i,0}$ one can rewrite A_i in a different fashion, namely,

$$A_i = \begin{cases} (b_i + \alpha_i)(R_{i,0}^{ma} - 1) + \left(\pi_i \sigma_{i,ma} - \dfrac{r_i}{K_i}\right) u_i, \\ \quad \text{density-dependent transmission,} \\ (b_i + \alpha_i)(R_{i,0}^{pm} - 1) - \dfrac{r_i}{K_i} u_i, \\ \quad \text{frequency-dependent transmission.} \end{cases}$$

Clearly some conclusions can be drawn concerning the stability of $(P_1^*0, 0, P_2^*, 0, 0)$ and the propagation of FeLV between two populations having small positive emigration and exchange rates for infectious individuals. First, if incidence in population i is frequency-dependent with $R_{i,0}^{pm} > 1$, then $(P_1^*0, 0, P_2^*, 0, 0)$ is not stable when $u_i \leqslant 0$ or small enough. Thus, FeLV can actually propagate from a village where it is endemic to any neighbouring population as soon as the dispersal process for susceptible individuals decreases population size in the village. Next, if incidence in population i is density-dependent with $R_{i,0}^{ma} < 1$, then $(P_1^*0, 0, P_2^*, 0, 0)$ becomes unstable when $u_i > 0$ is large enough, provided $(\pi_i \sigma_{i,ma} - (r_i/K_i)) > 0$ (which is likely to hold for most cat populations). Thus, even though FeLV would not propagate within two isolated populations, one of them being a farm, this can be achieved if the size of the farm population can be suitably increased by dispersal of susceptible individuals. Conversely, still assuming a density-dependent incidence in population i with $R_{i,0}^{ma} > 1$, then $(P_1^*0, 0, P_2^*, 0, 0)$ can become stable when $u_i < 0$ is large enough, provided $(\pi_i \sigma_{i,ma} - (r_i/K_i)) > 0$. Thus, FeLV can be eradicated from a farm where it is persistent upon connecting it to a larger population where incidence is frequency-dependent. The following case studies illustrate the above results and examine the consequences of the class of individuals dispersing, of the rate of dispersal and of the structure of the connected populations.

5.2.1. *The village–farm model*

Fig. 4 illustrates the village–farm model and compares the dispersal of non-infectious versus infectious animals. We use parameter values estimated previously (Fromont et al., 1998b), except for $\sigma_{ma} = 0.11$, which is chosen in order to set the threshold for FeLV extinction to $K = 45$ (from the definition of R_0^{ma}). The rates of dispersal are taken in accordance with field observations (Liberg et al., 2000). We assume that immune cats, which have a normal life, have the same dispersal rate than susceptible cats. With this set of parameters, when considering no exchange between the two populations ($c_{12}^k = c_{21}^k = 0$), FeLV develops in the village and goes extinct from the farm. When the two populations are connected through the exchange of either susceptible and immune cats ($c_{12}^X = c_{12}^Z = 0.05$, $c_{21}^X = c_{21}^Z = 0.02$, Fig. 4a) or infectious cats only ($c_{12}^Y = 0.05$, $c_{21}^Y = 0.02$, Fig. 4b), FeLV persists

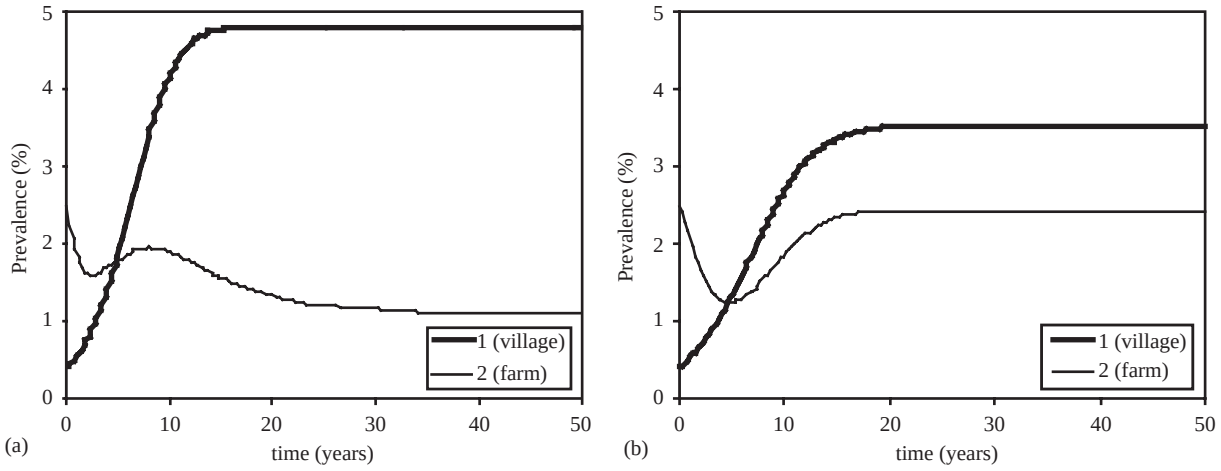

Fig. 4. Time evolution of the prevalence (Y_i/P_i) of FeLV viremia in a village–farm model. Common parameter values are $b = 0.88$ females.female.yr^{-1}, $m = 0.51\,\mathrm{yr}^{-1}$, $\pi = 0.33$ and $\alpha = 0.76\,\mathrm{yr}^{-1}$ for the two populations. Specific parameter values are $K_1 = 250$, $\sigma_{pm} = 6$, $i_{01}^k = e_{10}^k = 0$, $k = X, Y, Z$ for the village (population 1) and $K_2 = 40$, $\sigma_{ma} = 0.11$, $i_{02}^k = e_{20}^k = 0$, $k = X, Y, Z$ for the farm (population 2). At $t = 0$ each population contains $K - 1$ susceptible cats and 1 viraemic cat. Without connection between populations, FeLV persists in the village ($R_{1,0}^{pm} = 1.21$) but goes extinct from the farm ($R_{2,0}^{ma} = 0.89$). In (a) connection involves susceptible and immune cats, i.e., $c_{ij}^Y = 0$, $c_{12}^X = c_{12}^Z = 0.05$ and $c_{21}^X = c_{21}^Z = 0.02$. In (b), connection only involves infected cats, i.e., $c_{ij}^X = c_{ij}^Z = 0$, $c_{12}^Y = 0.05$ and $c_{21}^Y = 0.02$.

in both population. However, overall prevalence is lower when dispersers are infectious (3.36%) than when they are susceptible or immune (3.94%). Also, the difference between prevalences in the two populations is lower when dispersers are infectious than when they are susceptible or immune.

Fig. 5 shows the influence of the rate of dispersal from the village to the farm on prevalence of viraemia and on depression of host population size when $c_{21}^X = c_{21}^Z = 0.02$. Here dispersal involves susceptible and immune cats. Fig. 5a shows that when the rate of dispersion from the village to the farm is low ($c_{12}^X = c_{12}^Z \leqslant 0.02$), FeLV goes extinct in the farm. Nevertheless, prevalence in the village rises with the rate of exchange $c_{12}^X = c_{12}^Z$. When the rate of dispersion from the village to the farm stands above 0.03, FeLV is able to persist in the farm also and both prevalences keep rising with $c_{12}^X = c_{12}^Z$. However, prevalence is always lower in the farm compared to the village, and it is necessary to have $c_{12}^X = c_{12}^Z \geqslant 0.08$ so that there is at least one infectious individual in the farm at equilibrium. Fig. 5b shows that depression of host population size also increases with c_{12}^X. It is noteworthy that, even at low exchange rates when FeLV does not persist in the farm, both population sizes are lowered by FeLV, due to exchanges between the infected village and the virus-free farm.

5.2.2. The farm–farm model

Fig. 6a illustrates the farm–farm model. We consider a system of two farms where both R_0 are below unity and where the two populations are connected only through dispersal of non-infectious cats. A system with $K_1 = 40$, $K_2 = 42$, $c_{12}^X = c_{12}^Z = 0.15$ and $c_{21}^X = c_{21}^Z = 0.05$ allows for persistence of FeLV in population 2 only because dispersal increases the size of population 2 and decreases the size of population 1. Notice that overall prevalence and depression now equal only 0.20% and 0.84%, respectively.

5.3. Model with matrix

Here we consider the case of two populations with immigrating infectious individuals, i.e., we assume

$$\text{(H7)}\quad X_0(t) = X_0 \geqslant 0,\ Y_0(t) = Y_0 > 0, Z_0(t) = Z_0 \geqslant 0,\ t \geqslant 0 \text{ and either } i_{01}^Y > 0 \text{ or } i_{02}^Y > 0.$$

The dynamics of FeLV propagation is governed by the full set of ordinary differential equations given in (3). The existence and stability of a non-trivial stationary state (P_1^*, P_2^*) with positive components is analysed above. Again, the state $(P_1^*, 0, 0, P_2^*, 0, 0)$ does not exist anymore when condition (H7) holds because of the positive input of infectious individuals from the matrix; as a consequence, FeLV persists when condition (H7) is satisfied.

Note that when both $i_{0i}^Y = 0$ it is also possible for FeLV to persist within two connected populations having both a R_0 below unity, provided a suitable supply of susceptible individuals immigrate from the matrix, i.e. one of either $i_{01}^X > 0$ or $i_{02}^X > 0$ large enough and $X_0 > 0$. Fig. 6b illustrates this case in the same situation as in Fig. 6a except $i_{01}^X = i_{01}^Z = 0.15$ with $X_0 = 100$ and $Z_0 = 20$. Then FeLV is able to persist in both farms: persistence in farm 1 is due to immigration from the matrix and persistence in farm 2 is due to exchanges with farm 1. Comparing Figs. 4a, 6a and 6b shows that

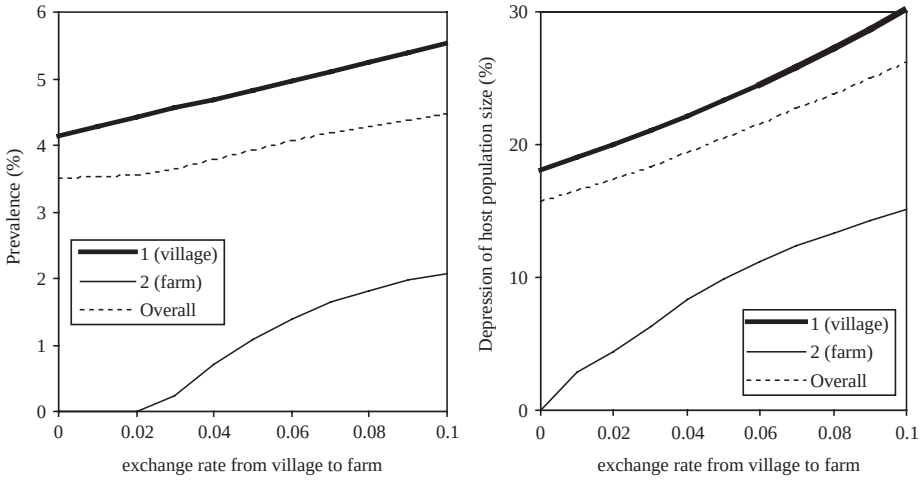

Fig. 5. Prevalence at equilibrium and depression of host population size at equilibrium depending on $c_{12}^X = c_{12}^Z$, when $c_{21}^X = c_{21}^Z = 0.02$ in a village–farm model. Other parameter values are set as in Fig. 4.

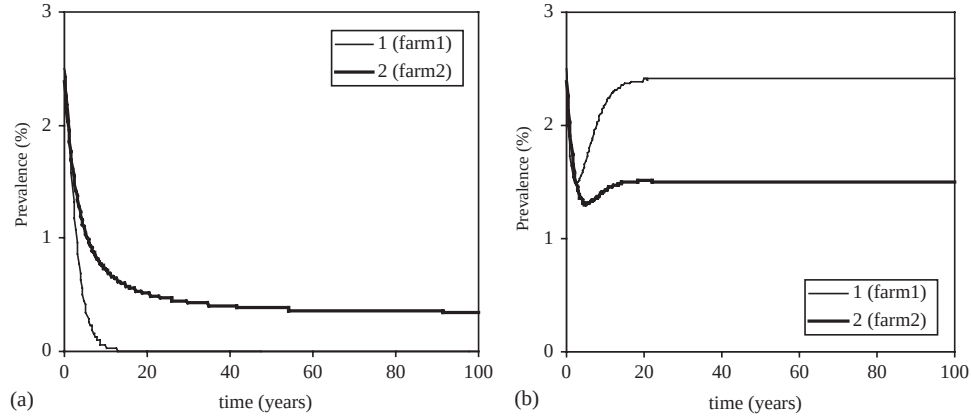

Fig. 6. Time evolution of the prevalence of FeLV viremia in a farm–farm and in a farm–farm–matrix models. Unless otherwise mentioned, parameter values and initial conditions are set as in Fig. 4. In (a) a farm–farm model is considered; carrying capacities are $K_1 = 40$ ($R_0^{ma} = 0.89$) and $K_2 = 42$ ($R_0^{ma} = 0.93$). Exchange only involves susceptible cats with $c_{12}^X = c_{12}^Z = 0.15$ and $c_{21}^X = c_{21}^Z = 0.05$. In (b) a farm–farm–matrix model is considered; parameters are set as in (a) except $i_{01}^X = i_{01}^Z = 0.15$ with $X_0 = 100$ and $Z_0 = 20$.

prevalence in a farm is higher when the farm is connected to a village or the matrix than when it is connected to another farm.

6. Discussion

Models taking into account the spatial structure of host-parasite systems have been proposed early (Bailey, 1975; May and Anderson, 1984). Our two-population model is in the spirit of the general model developed in Bailey (1975, pp. 351–353), who already used frequency-dependent transmission within populations and dispersal between populations. In earlier models, however, either formal investigation was lacking (Bailey, 1975), or models concerned populations having identical local dynamics (Jansen and Lloyd, 2000), or adaptation to a specific host-parasite system was incomplete (Faddy, 1986). Moreover, earlier models did not combine dispersal with density-dependent host population dynamics, nor separated the effects of dispersal of susceptible or infectious hosts. We introduced these features in the FeLV-cat model because data from a long-term monitoring suggest that they are biologically relevant. However, because we found unexpected results, we advocate that the specific effect of these hypotheses, the generic behaviour of such models and their biological relevance for other host-parasite systems should be investigated.

Our model implicitly assumes specific conditions for dispersal: the dispersal rate represents the rate of "effective migration", i.e., the rate at which individuals successfully settle in another population. Dispersal only depends on the disease status of dispersers, this means that the departure rate is not density-dependent, however the absolute number of cats leaving the population depends on population size. In the population where dispersers settle, they behave like native

individuals. In particular, their mortality is density-dependent. Surviving after settling down in a population is thus easier when numerous home ranges are left vacant by native cats, for example when FeLV regularly kills native individuals, which seems a realistic assumption.

Concerning disease persistence, our results conform to the general prediction that spatial heterogeneity should promote persistence in host-parasite systems (Andreasen and Christiansen, 1989; Wood and Thomas, 1996; Jansen and Lloyd, 2000). However, dispersal may also favour the local extinction of the virus from small populations, when they are connected to larger ones. We distinguish two possible mechanisms explaining persistence. When infectious cats disperse then persistence occurs without condition. On the contrary, when dispersal only involves susceptible individuals, the dispersal process must act to increase the size of farms at the expense of villages, for disease to persist in farms. This condition means that dispersal must be asymmetric: the rate of effective dispersal toward small populations should be higher than toward villages. Our model thus predicts that the attractiveness of large populations may prevent disease persistence in small populations.

Our outstanding conclusion is that dispersal has other consequences than FeLV persistence only. First, the level of the predicted prevalences is not the same according to the kind of population structure considered. Even if quantitative outputs can only be used as guidelines because we did not estimate field transmission rates, prevalences predicted for farms are lower in the case of farm–farm systems than in farm–village or farm–matrix combinations. In the field, when farms are connected to villages or when several surrounding populations lead to high numbers of feral cats roaming between populations, FeLV could be continuously present in the farm. On the contrary, when only farms are connected to each other, the predicted persistence at low prevalence may probably be expressed as successive extinctions and recolonizations. Secondly, dispersal influences FeLV prevalence and its impact on host population growth independently from FeLV persistence. For example, in the village–farm model, when susceptible cats have low dispersal rates, persistence is not achieved in the farm, however FeLV prevalence in the village is related to the rate of dispersal. As a consequence, the depression of host population size due to FeLV increases as soon as dispersal occurs, whether or not disease persistence is achieved. Particularly, a depression is observed in the farm where FeLV does not persist. We hypothesize that this effect results from the combination of dispersal with density-dependent population dynamics: the farm "gives" cats to compensate the impact of disease in the village. This prediction has important consequences regarding the dynamics of small populations: disease may affect population dynamics even when it is not present in the population but only in surrounding connected populations.

Finally, important consequences derive from the category of individuals dispersing. Beside the influence on FeLV persistence discussed above, the disease status of dispersers influences virus prevalence. The overall prevalence is lowered when infectious cats disperse, compared to the case when non-infectious disperse. In other words, prevalence is more sensitive to the dispersal rate of non-infectious than to that of infectious. However, one must notice that, with similar dispersal rates, the absolute number of non-infectious dispersers is higher than the absolute number of infectious dispersers. Probably, the dispersal of susceptible individuals displaces the reservoir of the disease while the dispersal of infectious displaces the virus itself. Moreover, the dispersal of infectious cats decreases the difference between prevalences in the village and in the farm. This result is in agreement with the analysis of disease persistence: the dispersal of infectious equilibrates disease levels of the connected populations more efficiently than the dispersal of susceptibles.

As a conclusion, with minimal biological hypotheses, we predict that important changes arise as soon as host populations are connected through dispersal: the impact of disease on host population growth increases and disease may act on distant populations through dispersal, even when persistence is not achieved. Moreover, because these conclusions prove to be sensitive to the dispersal rate and to the class of individuals dispersing, we hypothesize that taking into account more details of the dispersal process would possibly modulate the predictions of the model. For example, other characteristics than infection status could differentiate dispersers from non-dispersers, such as their behaviour, body condition, social rank, thus modifying their contact rate, reproductive success or survival. The characteristics of populations could also determine their attractiveness (Clobert et al., 2001) and dispersal may then be dependent on the information that individuals can gain about their environment: for example a susceptible cat would benefit from leaving a heavily infected population to join a healthier one. To precisely determine the influence of dispersal in the cat-FeLV or other host-parasite systems, we now need to better take into account field characteristics of dispersion, to consider more realistic functions in the model.

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Appendix A. Stability analysis of disease free states

A.1. Population dynamics in the absence of virus

Some basic generic results for (4) can be quickly derived. The system of ordinary differential equations in (4) can be conveniently rewritten $P_1' = f_1(P_1, P_2), P_2' = f_2(P_1, P_2)$.

One may observe that trajectories starting a time $t = 0$ from $P_i(0) \geqslant 0$, $i = 1, 2$ remain nonnegative at later times, $P_i(t) \geqslant 0$, $i = 1, 2$, $t \geqslant 0$, and are globally bounded. One can check that no periodic trajectory with positive components can exist; this follows from the Bendixson-Dulac criterion: a straightforward computation shows

$$\frac{\partial}{\partial P_1}\left[\frac{1}{P_1 P_2} f_1(P_1, P_2)\right] + \frac{\partial}{\partial P_2}\left[\frac{1}{P_1 P_2} f_2(P_1, P_2)\right] < 0.$$

Local stability analysis for a given stationary solution of (4) is performed upon evaluating a Jacobian matrix there; one has

$$J(P_1, P_2) = \begin{pmatrix} r_1 - 2\frac{r_1}{K_1}P_1 - (c_{12}^X + e_{10}^X) & c_{21}^X \\ c_{12}^X & r_2 - 2\frac{r_2}{K_2}P_2 - (c_{21}^X + e_{20}^X) \end{pmatrix}.$$

Let us begin with the trivial state (0,0). Then, assuming (H1) is satisfied, (0,0) is feasible and it is LAS provided the trace of $J(0,0)$ be negative and its determinant be positive; a direct substitution yields condition (C1). Next, when (H1) and (C1) are fulfilled, no semi-trivial stationary states, i.e. $(0, P_2^*), (P_1^*, 0), P_i^* > 0$, $i = 1, 2$, can exist. Looking for stationary states with positive components, when (H1) holds, null clines for (4) or (A.1) reads

$$P_2 = \frac{1}{c_{21}^X}\left[\frac{r_1}{K_1}P_1^2 + (c_{12}^X + e_{10}^X - r_1)P_1\right],$$

$$P_1 = \frac{1}{c_{12}^X}\left[\frac{r_2}{K_2}P_2^2 + (c_{21}^X + e_{20}^X - r_2)P_2\right],$$

a graphical analysis shows these two quadratic functions do not intersect inside the positive orthant $(P_1, P_2), P_1 > 0, P_2 > 0$,as long as condition (C1) holds, condition (C1.3) giving the respective positions of the clines at the (0,0). Hence (0,0) is the unique stationary state when (H1) and (C2) are both fulfilled; this together with previous generic results for trajectories of (4) yields global stability.

Next, a semi-trivial stationary state $(P_1^*, 0), P_1^* > 0$ is feasible if and only if (H3) holds, in which case it is uniquely defined. The Jacobian matrix $J(P_1^*, 0)$ shows it is LAS when $r_2 - e_{20}^X - c_{21}^X < 0$. Now, when (H3) and $r_2 - e_{20}^X - c_{21}^X < 0$ hold, a direct analysis of the differential equation for P_2 in (4) that is independent of P_1 shows $P_2(t) \to 0$ as $t \to +\infty$, exponentially; substituting this back into the equation for P_1 in (4), one easily gets $P_1 \to P_1^*$ as $t \to +\infty$, yielding global stability. In the limiting case $r_2 - e_{20}^X - c_{21}^X = 0$, a graphical analysis of the equation for P_2 first, and then of the equation for P_1 supplies the same GAS result. A similar analysis can be carried out for a semi-trivial state $(0, P_2^*), P_2^* > 0$.

We now handle stationary states with positive components, $(P_1^*, P_2^*), P_1^* > 0, P_2^* > 0$. A graphical analysis shows that such a state exists and is unique in the four situations described in the Results section. In the first case where (H2) holds, the logistic type differential equation for P_1 in (4) is independent of P_2 and P_0; hence, when $r_1 - e_{10}^X - c_{12}^X > 0$ one has $P_1(t) \to K_1$ as $t \to +\infty$, exponentially; substituting this back into the equation for P_2 in (4), one easily gets $P_2(t) \to P_2^* > 0$ as $t \to +\infty$, yielding global stability. A similar analysis holds for the case where (H3) holds and $r_2 - e_{20}^X - c_{21}^X > 0$. In the third case, when (H4) holds, no trivial or semi-trivial stationary state can exist; global stability for $(P_1^*, P_2^*), P_1^* > 0, P_2^* > 0$ follows from uniqueness and previous generic results. In the last case, looking at the Jacobian matrix yields local stability; a graphical analysis of null clines gives global stability.

A.2. Derivation of condition (C2)

The LAS condition (C2) for the disease free state $(P_1^*, 0, 0, P_2^*, 0, 0)$ is derived upon looking at the Jacobian matrix of system (3); this matrix is sparse but a lot of algebra is required. A more convenient way is to reorder the equations in system (3) along the state variables $(X_1, X_2, Z_1, Z_2, Y_1, Y_2)$, and modify the system into: $X_i' = f_i\ (X_1, X_2,\ Z_1, Z_2, Y_1, Y_2)$, $i = 1, 2$, $Z_i' = g_i(X_1, X_2, Z_1, Z_2, Y_1, Y_2)$, $i = 1, 2$, $Y_i' = h_i(X_1, X_2, Z_1, Z_2, Y_1, Y_2)$, $i = 1, 2$. Now we are to look at the local stability of the stationary state $(P_1^*, P_2^*, 0, 0, 0, 0)$ for this reordered system, (P_1^*, P_2^*) being the unique persistent state of (5). The Jacobian matrix of this reordered system evaluated at $(P_1^*, P_2^*, 0, 0, 0, 0)$ is a upper block triangular matrix

$$\begin{pmatrix} J_{11} & J_{12} & * & * & * & * \\ J_{21} & J_{22} & * & * & * & * \\ 0 & 0 & J_{33} & J_{34} & * & * \\ 0 & 0 & J_{43} & J_{44} & * & * \\ 0 & 0 & 0 & 0 & J_{55} & J_{56} \\ 0 & 0 & 0 & 0 & J_{65} & J_{66} \end{pmatrix},$$

herein * are entries of no use for the stability analysis. Using (5), direct substitution yields

$$\begin{pmatrix} J_{11} & J_{12} \\ J_{21} & J_{22} \end{pmatrix} = \begin{pmatrix} -\frac{(c_{21}^X P_2^* + i_{01}^X P_0)}{P_1^*} & c_{21}^X \\ c_{12}^X & -\frac{(c_{12}^X P_1^* + i_{02}^X P_0)}{P_2^*} \end{pmatrix},$$

$$\begin{pmatrix} J_{33} & J_{34} \\ J_{43} & J_{44} \end{pmatrix} = \begin{pmatrix} -(m_1 + c_{12}^Z + e_{10}^Z) & c_{21}^Z \\ c_{12}^Z & -(m_2 + c_{21}^Z + e_{20}^Z) \end{pmatrix},$$

$$\begin{pmatrix} J_{55} & J_{56} \\ J_{65} & J_{66} \end{pmatrix} = \begin{pmatrix} A_1 - (c_{12}^Y + e_{10}^Y) & c_{21}^Y \\ c_{12}^Y & A_2 - (c_{21}^Y + e_{20}^Y) \end{pmatrix}.$$

The first two matrices have negative traces and positive determinants; they are stable matrices. For the last one it has a negative trace and a positive determinant provided condition (C2) holds, which completes the stability analysis proof.

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