When domestic cat (*Felis silvestris catus*) population structures interact with their viruses

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Appendix

This mathematical model is an extension of the classical Susceptible-Infected (*SI*) model. Cats are classified into two epidemiological classes, the first one representing susceptible individuals (*S*) and the second one representing FIV infected cats (*I*). The model distinguishes between orange cats and non-orange cats. For the sake of simplicity, we assume non-sexual reproduction between individuals. Orange and non-orange cats give birth to kittens only of the same colour, respectively. Classes are divided into two subclasses to account for host polymorphism. A subscript '1' is used for non-orange cats and a subscript '2' denotes orange cats.

b_1 and b_2 are the birth rates of non-orange and orange cats, respectively. All susceptible cats die with the same rate $m+eN$, whatever their genotype, where m is the density-independent mortality rate of cats and e is the density-dependent coefficient of the death rate, i.e. the natural death rate of individuals increases linearly with the density of the population. Using a density-dependent term for the mortality rate is a convenient and simple way to limit the host population growth rate. The carrying capacity of the population for genotype X (K_X), i.e. the host population equilibrium size in the absence of the virus and with genotype X alone, is then $K_X=(b_X-m)/e$. Since recovery from FIV is impossible, cats only leave the I class when they die, with a rate $m+eN+a$, where a is the additional mortality rate induced by FIV.

We call β the transmission rate of the virus, i.e. the rate at which infected non-orange cats have infectious contacts with other individuals. We assume that this transmission rate does not depend on the population size, i.e. each individual will have the same number of contacts with other individuals whatever the host population size, a natural assumption for social species like cats (Liberg et al. [11]). We assume that orange cats have q times more at-risk contacts with other individuals than non-orange cats.

The model then reads:

$$\lambda = \beta \frac{I_1 + qI_2}{N_1 + qN_2}$$

$$\frac{dS_1}{dt} = b_1 N_1 - (m + eN)N_1 - \lambda S_1$$

$$\frac{dS_2}{dt} = b_2 N_2 - (m + eN)N_2 - q\lambda S_2$$

$$\frac{dI_1}{dt} = \lambda S_1 - (m + eN + a)I_1$$

$$\frac{dI_2}{dt} = q\lambda S_2 - (m_R + eN + a)I_2$$

where $N_1 = S_1 + I_1$ is the total number of non-orange cats, $N_2 = S_2 + I_2$ is the total number of orange cats and $N = N_1 + N_2$ is the total number of cats in the population.

The model is analyzed with numerical simulations using plausible values for the parameters. Time units are measured in years. The life expectancy of cats, whatever their genotype, is 10 years ($m=0.1$) in the absence of competition for resources. Note that this value is not representative of the cat mortality rate since, in simulations, density-dependent effects are important, causing the overall mortality (including both natural and FIV-induced mortality rates) to compensate for the birth rate, such that in disease-equilibrium the life expectancy of non-orange cats (when they make up 100% of in the population) is around 4 years ($b_1=1/4$ years). Orange cats have a greater reproductive rate b_2 so, since all cats have the same basic mortality rate, they have a selective advantage b_2/b_1 in disease-free conditions where the fitness of a cat is proportional to its reproductive rate. The additional mortality rate due to FIV is set to $a = 1/40$: at equilibrium the life expectancy (and thus the fitness) of non-orange cats decreases by around 10%.due to FIV. Obviously FIV can balance the fitness advantage of orange cats only if this advantage is smaller that the maximum fitness cost of FIV. This constrains the selective advantage of orange cats to a range $1 < b_2/b_1 < 1.1$. Finally, some parameters (β, q and b_2) are undetermined and so we consider different values for them.

To analyse the model we look at the state in which the system attains equilibrium. Because the orange mutation is ancient, it is reasonable to assume that competition between these two genotypes has reached equilibrium (at least on a global scale; within populations the frequency of each genotype is submitted to random fluctuations). We use numerical simulations to estimate the solutions of the differential equation system. We consider initial conditions where the number of non-orange and orange cats is half of the carrying capacity of the population for non-orange and orange cats, respectively. At time $t=0$ we introduce one infected non-orange cat into the population.

Fig. 1 shows the characteristics of the system under different parameters. We first consider a selective advantage for orange cats $b_2/b_1 = 1.05$ with a transmission rate $\beta = 0.1$ and look at different values of the relative transmission rate (q). Fig.1a illustrates the existence of three regions for q. For $q < 9$, orange cats are always selected for. In this instance, the additional mortality induced by FIV in

orange cats is not great enough to balance their larger reproductive rate. For $q > 9$, the pressure exerted by FIV endows a selective advantage on non-orange cats. The impact of FIV depends on the proportion of orange cats in the population. A larger proportion of orange cats will increase the impact of FIV, especially on that colour morph. Thus, FIV has a density-dependent impact that helps maintain the polymorphism between the two genotypes. In practice, long-term persistence of the polymorphism can be observed only for $9 < q < 20$. For $q > 20$, the equilibrium proportion of orange cats is almost zero.

To check for consistency between the model outcome and real systems, we also plot the equilibrium prevalence of FIV in each genotypic group (Fig. 1b). Of course the prevalence of FIV in non-orange cats makes sense only if they are present in the population (so only for $q > 9$). In the model space where the two genotypes can coexist, the prevalence of FIV is approximately 10% in non-orange cats compared to approximately 60% in orange cats, the latter value being much larger than usually observed (~30%, Pontier et al. [57]).
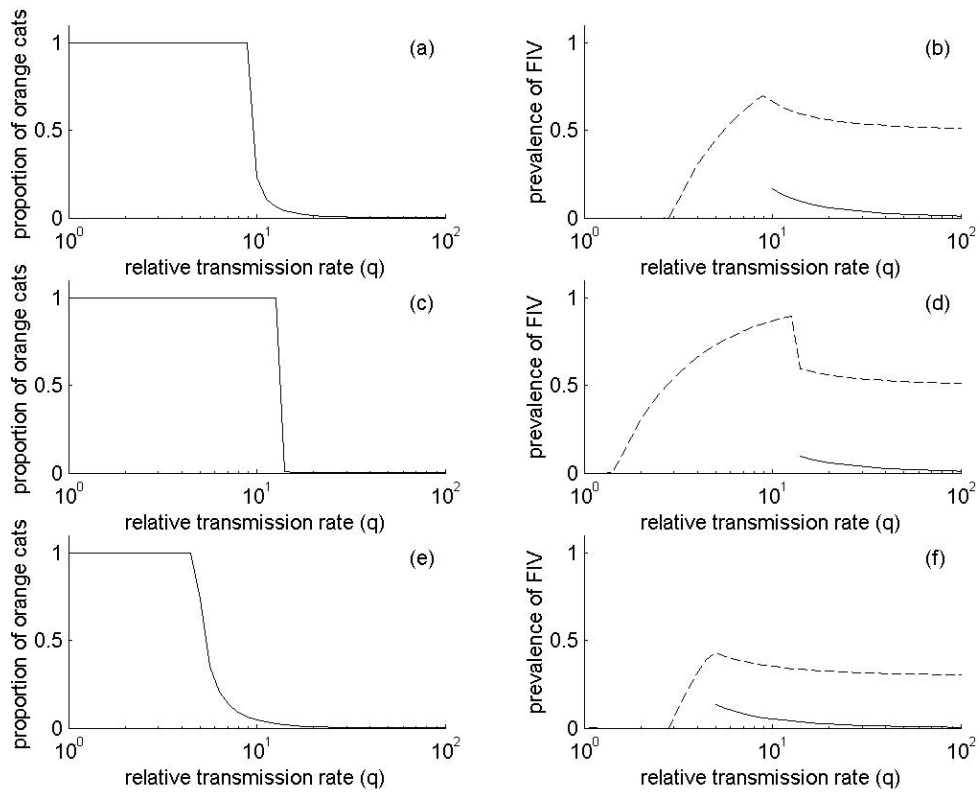

Fig.1: Long term evolution of the system according to the relative transmission rate of FIV in orange cats (q). In (a), (c) and (e) the Y-axis represents the proportion of orange cats in the cat population at equilibrium. In (b), (d) and (f) the Y-axis is the prevalence of FIV in orange (dashed lines) and non-orange cats (solid lines) at equilibrium. (a) and (b) $\beta = 0.1$ and $b_2/b_1 = 1.05$; (c) and (d) $\beta = 0.2$ and $b_2/b_1 = 1.05$; (e) and (f) $\beta = 0.1$ and $b_2/b_1 = 1.03$.

We repeated the same *in silico* experiment for a larger transmission rate ($\beta = 0.2$, Figs.1c, d). Here, there is almost no area of model space where the two genotypes can coexist. Coexistence can only be observed when the transmission rate of FIV is small enough to permit a small impact of FIV in non-orange cats.

Next we look at what happens when we consider a smaller selective advantage for orange cats ($b_2/b_1 = 1.03$, Figs. 1e, f). Results are similar to those outlined above (see Figs. 1a, b), except for the area of coexistence, which is larger ($4 < q < 20$).

Finally we investigate two parameters (β and b_2/b_1) in more detail (Fig. 2). In rural populations the proportion of orange cats is approximately 20% (Pontier et al. [13]). For each value of β and b_2/b_1, we consider the value of q for which the proportion of orange cats is 20% (Figs 2a, c). We then look at the prevalence of FIV in each genotypic group for the corresponding value of q ((Figs.2b, d).
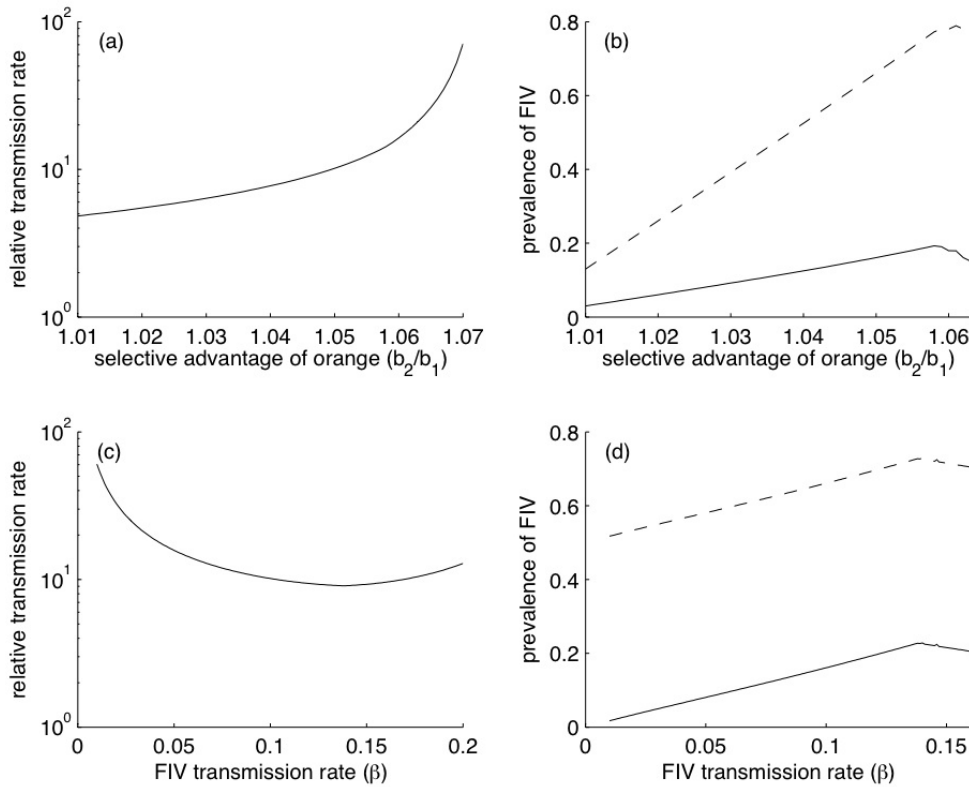

Fig. 2: Characterization of the equilibrium states in which the proportion of orange cats in the population is 20%. In (a) and (c) the Y-axis represents the value of the relative transmission rate (q). In (b) and (d) the Y-axis represents the prevalence of FIV in orange (dashed lines) and non-orange cats (solid lines). (a), (b) According to the selective advantage for orange cats (b_2/b_1), with a fixed transmission rate ($\beta = 0.1$); and (c), (d) according to the FIV transmission rate (β), with a fixed selective advantage of orange cats ($b_2/b_1 = 1.05$).

4

First we look at different values for the selective advantage of orange cats (b_2/b_1), considering a fixed transmission rate ($\beta = 0.1$). For $b_2/b_1 > 1.07$, orange cats are always selected for. The impact of FIV is not large enough to balance this fitness advantage. For $b_2/b_1 < 1.06$, the prevalence of FIV expected by the model (considering that the population stabilises at 10% of orange cats) increases linearly with b_2/b_1. Note that for $b_2/b_1 = 1.023$ the expected prevalence of FIV is 7% for non-orange cats and 30% for orange ones, which is quite close to what we observe in the field (Pontier et al. [57]). The prevalence of FIV is at a maximum for $b_2/b_1 = 1.06$, where 15% of non-orange and 75% of orange cats are infected. For $1.06 < b_2/b_1 < 1.07$, the expected prevalence of FIV is decreasing in non-orange cats and constant in orange ones. Note that each point is obtained for different values of q. For greater values of selective advantage for orange cats, the relative transmission rate (q) required to observe a proportion of 10% of orange cats in the population at equilibrium becomes larger (Fig. 2a). Note that even when orange cats have a selective advantage as small as 1.01, they must have at least six times more at-risk contacts than non-orange cats to obtain the observed distribution between genotypes.

We obtain similar results for the transmission rate (β, Fig 2c, d), considering a fixed selective advantage for orange cats ($b_2/b_1 = 1.05$). Here, the prevalence of FIV in both genotypic groups increases initially and then decreases with β, and is maximum for $\beta = 0.15$. Again the relative transmission rate (q) must be high ($q > 10$) to obtain the observed proportion of orange cats in the population.