Deterministic homogenous-mixing model

The model is based on the following set of ordinary differential equations:

$$N = M + S + I + I_M + R_1$$

$$\Lambda = \beta \frac{I + \rho I_M}{N}$$

$$\frac{dM}{dt} = b(N - S) - (\mu_0 + \delta N)M - q\Lambda M - wM$$

$$\frac{dS}{dt} = bS + wM - (\mu_0 + \delta N)S - \Lambda S$$

$$\frac{dI}{dt} = \Lambda S - (\mu_0 + \delta N + \alpha + \sigma)I$$

$$\frac{dI_M}{dt} = q\Lambda M - (\mu_0 + \delta N + \alpha_M + \sigma_M)I_M$$

$$\frac{dR_1}{dt} = \sigma I + \sigma_M I_M - (\mu_0 + \delta N)R_1$$

Here there is no superscript *k* since there is only one subpopulation. The model being deterministic, global extinction of the pathogen never happens and so the external reintroduction term does not have to be considered.

Using this model, and for the basic value of the parameters, we can calculate the number of individuals infected by each form of the disease every year at the equilibrium (Figure ESM1). The basic value of the transmission rate (β_0=100) corresponds to a situation where the annual number of severe diseases is highly reduced (130) compared to its maximum (527). The intense circulation of the pathogen limits its impact.

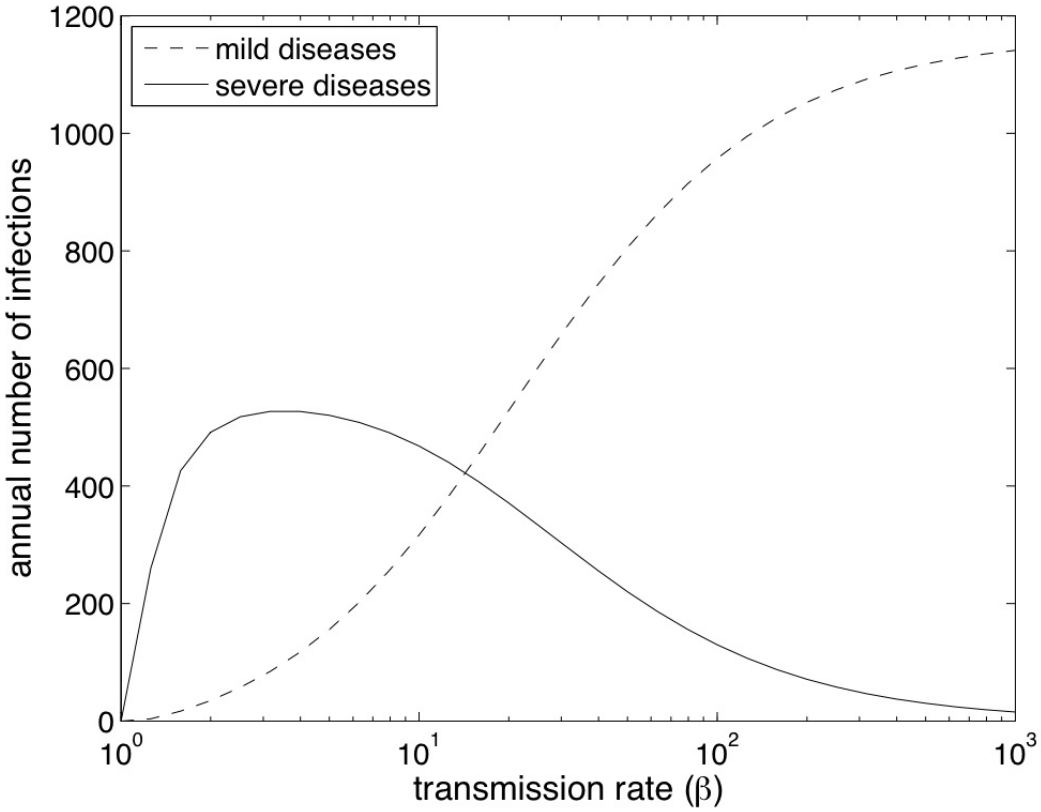

Figure ESM1: number of individuals infected by the severe (solid line) or the mild (dashed line) form of the disease every year at the equilibrium, according to the local transmission rate.

Estimation of extinction and re-introduction times

Estimating both extinction and reintroduction times from the simulations is not straightforward. A tempting solution would be to keep track of all extinction and reintroduction events for each subpopulation and each replicate. One could then estimate how long it takes on average for the virus to locally fade out and to be reintroduced. Unfortunately, all periods last only for 10 years (8 years if we remove the first 2 years). At the end of the period some events (extinctions or reintroduction) have not happened yet. Simply removing them from the estimation would clearly introduce a bias (in

particular estimations would necessarily be below 8 years). Hence we estimate these quantities by the following two methods.

Persistence time: to estimate the persistence time during the course of the fragmentation, we have considered equivalent (i.e., same size) isolated subpopulations. This does not have a large impact on the estimate since when at least one individual is infected in the subpopulation it is 100 times more infectious than any infected individual in a neighbouring subpopulation. As long as the pathogen is present in the subpopulation, individuals in neighbouring subpopulations play almost no role in transmission.

For each value taken by the carrying capacity of subpopulations during the course of the fragmentation process (i.e. $5*2^X$, where X is an integer between 0 and 8), we considered an initially disease-free subpopulation where $S=K$. At $t=0$ we introduce one (severely) infected individual. We continue the simulation until the pathogen goes extinct ($I+I_M=0$). We replicate this procedure 100 times and give the mean and confidence intervals of the persistence time.

Reintroduction time: Estimation of the reintroduction time cannot be made using the same method simply because it depends on the connectivity between all subpopulations. However, the mean time before reintroduction of the pathogen is given by the inverse of the reintroduction rate, which is simply given for each subpopulation k by:

$$(S^k + qM^k) \times \lambda\beta_0 \sum_{j \in \eta(k,t)} \frac{I^j(t) + \rho I_M^j(t)}{N^j}$$

The second term describes the force at which neighbours transmit the pathogen to the subpopulation. The first term is a measure of the susceptibility potential of the subpopulation.

We take the average of the re-introduction rate over time (the 8 last years of the considered 10 years period) and all subpopulations. Note that this gives the reintroduction rate of the pathogen in any subpopulation, even infected ones, which provides an estimate of reintroduction time even when subpopulations are infected. For an infected subpopulation, this estimate indicates how quickly the pathogen would be reintroduced on average if the pathogen was suddenly removed.

Using the formulae for the expectation of variance of a complex variable:

$$E(\frac{1}{V}) = \frac{1}{E(V)}(1 + \frac{\sigma^2(V)}{E(V)^2}),$$

we calculate the mean of inverse of the reintroduction rate (i.e. the reintroduction time). The confidence interval of the reintroduction time is then simply the inverse of the confidence interval of the reintroduction rate.

Differential impact of myxomatosis within the metapopulation

As the model is defined, all subpopulations are not equivalent. Edge subpopulations have less neighbours and so less opportunities to get re-infected. Is there a differential effect in the way they are affect by the pathogen?

To assess this question, we first look at the impact of the pathogen within each subpopulation for each of the 9 ten years period (Figure ESM2). This picture shows that the impact of the pathogen is homogeneous in space until the last fragmentation event. Then it becomes highly variable between subpopulations. This is because at this stage extinctions are frequent and reintroductions rare. The impact of the pathogen depends on

how often it is reintroduced from an external source, which is highly variable between subpopulations.

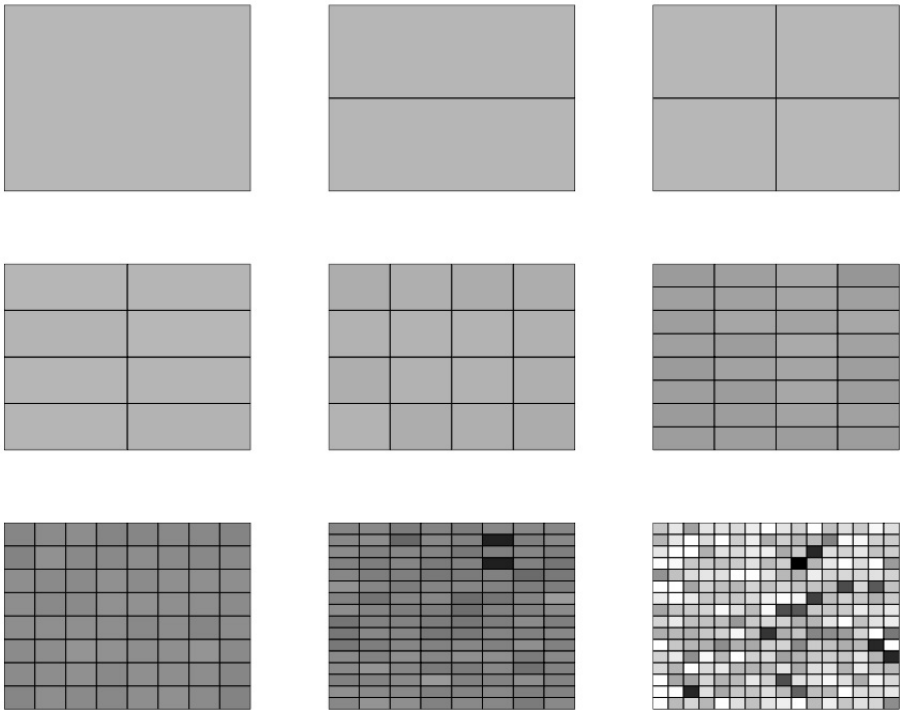

Figure ESM2: mean impact of the pathogen during the 8 last years of the 9 ten year periods. Black = maximal impact of the disease; white = the disease had no impact over the period. Intensity of grey is proportional to the impact of the disease.

Figure ESM2 does not demonstrate a difference in edge subpopulations. However, a clearer picture emerges when we plot the impact of the disease as a function of the number of neighbours (Figure ESM3). The 3 first 10 years periods are omitted because in these situations all subpopulations have the same number of neighbours.

Although the standard errors are large, due to the small number of edge subpopulations, results show a clear tendency. Initially, the impact of the pathogen

increases with the number of neighbours. However in the last years it decreases. This can be explained by the fact that increasing the number of neighbours increases the frequency of pathogen reintroductions. Initially increasing the number of neighbours has a beneficial effect because epidemics are then more severe; finally it is deleterious because epidemics are then more rare.

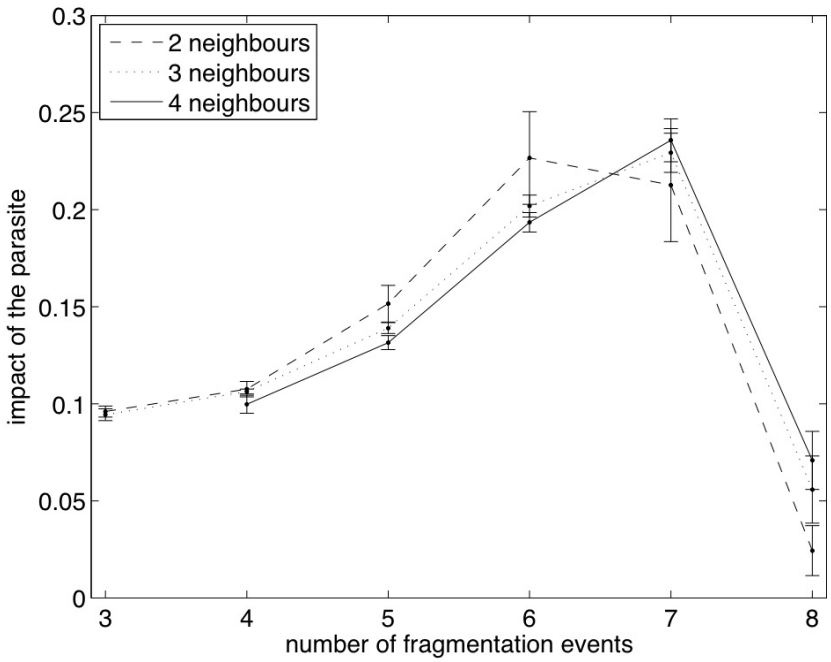

Figure ESM3: impact of the pathogen (mean and 95% confidence interval) according to the number of fragmentation events, within subpopulations in the corner (2 neighbours, dashed line), on the edge (3 neighbours, dotted line) and non-edging subpopulations (4 neighbours, solid line).