This is an electronic appendix to the paper by Gandon *et al*. 2003 Imperfect vaccination: some epidemiological and evolutionary consequences. *Proc. R. Soc. Lond.* B **270**, 1129—1136. (DOI 10.1098/rspb.2003.2370.)

Electronic appendices are refereed with the text. However, no attempt is made to impose a uniform editorial style on the electronic appendices.

Electronic Appendix A: Local and global stability of evolutionary equilibria

The pairwise invasibility plots (PIP) give the fate of a mutant (extinction or invasion) as a function of both mutant and resident strategies (figure 4). The mutant will invade if the sign of its instantaneous rate of increase is positive (i.e., when $Log[R[\alpha*,\alpha]] > 0$). This analysis allows a check on both the *local* and *global* evolutionarily stability of different virulence strategies (i.e. whether mutant strategies can invade a resident parasite population). Figure 4 shows that locally stable equilibria can be globally unstable. For example, in figure 4*c* the lower locally stable equilibrium is not globally stable since a resident population can be invaded by mutants with higher virulence. This means that the switch from the low equilibrium to the high one could occur for low vaccination coverage if more virulent mutants appear in the population.

These PIPs can also be used to analyse the potential coexistence between different virulence strategies. Indeed, if a mutant strategy, α_1, can invade a resident population with virulence α_2 *and* if a mutant strategy, α_2, can invade a resident population with virulence α_1, then strategies α_1 and α_2 can coexist. A geometric translation of this implies that when a PIP is symmetrical along the diagonal no polymorphism can be maintained. Such symmetry arises in the case where single infections occur (when $\sigma = 0$). In other words, when only single infections occur, two different strains can never coexist. On the other hand, when superinfection occurs (i.e. $\sigma > 0$) coexistence between different virulent strategies may occur (Pugliese 2002).

A. Host expected lifespan

Following van Baalen (1998), the probabilities of being in the four possible states of the host (susceptiple uninfected, *su*, susceptible infected, *si*, vaccinated uninfected, *vu*, vaccinated infected, *vi*) can be ordered in a vector $\boldsymbol{q}(a)$, which yields

$$\frac{d\,\boldsymbol{q}(a)}{d\,a} = \mathbf{A}\boldsymbol{q}(a)$$

where

$$\boldsymbol{q} = \begin{pmatrix} q_{su} \\ q_{si} \\ q_{vu} \\ q_{vi} \end{pmatrix}$$

and

$$\mathbf{A}=\begin{pmatrix} -\delta-h & 0 & 0 & 0 \\ h & -\delta-h-\alpha & 0 & 0 \\ 0 & 0 & -\delta-h' & 0 \\ 0 & 0 & h' & -\delta-h'-\alpha' \end{pmatrix}$$

The expected time spent in each state is given by

$$\int_0^\infty \boldsymbol{q}(a)da = \text{-}\mathbf{A}^{-1}\boldsymbol{q}(0)$$

with

$$\boldsymbol{q}(0)=\begin{pmatrix} 1\text{-}p \\ 0 \\ p \\ 0 \end{pmatrix}$$

This leads to

$$L[p,r_1,r_2]=\frac{(1-p)(\delta+h+\alpha)}{(\delta+h)(\delta+\alpha)}+\frac{p(\delta+h'+\alpha')}{(\delta+h')(\delta+\alpha')}$$

where h and h' are complicated functions of both host and parasite life cycles including parameters characterizing vaccination (i.e., p, r_1 and r_2).

Figure 5 presents an example which illustrates that maximum vaccination coverage may not always increase host expected lifespan. An increase of the vaccination coverage always yields higher expected host lifespans in the absence of virulence evolution (full line). However, when parasite virulence is allowed to evolve, the expected lifespan may be maximised for intermediate values of vaccination coverage (dashed line).

References :

Pugliese, A. (2002). On the evolutionary coexistence of parasite strains. *Math. Biosci.* **177&178**, 355-375.

van Baalen, M. (1998). Coevolution of recovery ability and virulence. *Proc. R. Soc. Lond.* B **265**, 317-325.

Figure 4: Pairwise Invasibility Plots (PIPs) of parasite virulence for increasing levels of vaccination coverage ($p = 0.2$, 0.3, 0.4 and 0.7 in ***a***, ***b***, ***c*** and ***d***, respectively). Each plot presents the sign of the instantaneous rate of increase of mutant with virulence α^* introduced in a monomorphic population of residents (with virulence α) at its epidemiological equilibrium. In the white area the mutant's rate of increase is positive (the mutant invades the resident population) while, in the black area, its rate of increase is negative (the mutant goes to extinction). Note that the rate of increase of the mutant is zero along the diagonal, where $\alpha = \alpha^*$. These PIPs can be used to find evolutionarily stable (and unstable) equilibria. The white circles show stable equilibria while the grey circles show unstable ones. The intermediate equilibrium is always unstable. Note that in figure ***c*** the lower evolutionary equilibrium is locally stable but not globally stable since a mutant with virulence $\alpha^* = 0.3$ can invade. Reciprocally, figure ***b*** presents a case where the higher evolutionarily equilibrium is not globally stable. When $\sigma = 0$ the symmetry of the PIP along the diagonal implies that the global stability of one locally stable equilibrium yields global instability of the other locally stable equilibrium. The instability of the different equilibria is indicated in figure 3. Here we used the same transmission function and the same parameter values as in figure 3*h*.

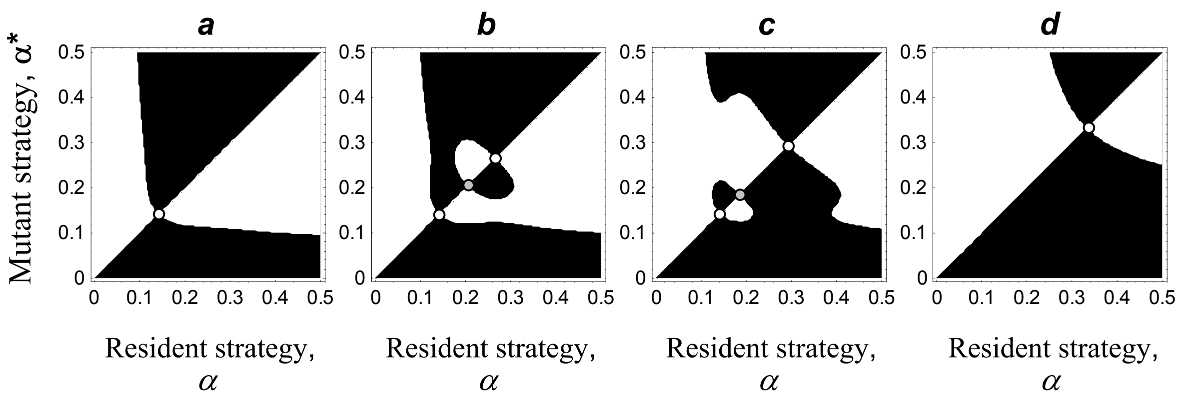

Figure 5: Expected lifetime of the host, $L[p, r_1, r_2]$, against vaccination coverage, p. The dashed line shows the case where the parasite adopts the evolutionarily stable virulence before vaccination and is not allowed to evolve after vaccination. The full line shows the case where the parasite virulence is allowed to evolve after vaccination. The parameter values are the same as the ones used for figure 3d.