Supporting information for Evolution of suicide as a defense strategy against pathogens in a spatially structured environment

1. Well-mixed model

Equation (1) in the main text gives the full epidemiological dynamics of the sytem. It can be used to understand the change of: $N = S + A + R$, the total density of bacteria. This equation, however, depends on the frequencies of the different types of defense strategies in the population. These frequencies are likely to change and equations (2) give the full evolutionary dynamics of the host population. These equations can be used to study the independent evolution of each type of defense strategy.

When altruistic resistance is absent ($f_A = 0$), the evolution of classical resistance is given by:

$$\frac{df_R}{dt} = f_R(1 - f_R)\big(abV - rc_R(1 - \kappa N)\big) \quad \text{(A1)}$$

This equation shows that the evolution of classical resistance is governed by the balance between the rate at which bacteria are exposed to the virus, abV, and the cost of resistance, $rc_R(1 - \kappa N)$. When the density of virus is sufficiently high, classical resistance is favored.

In contrast, when classical resistance is absent ($f_R = 0$), the evolution of altruistic suicide is given by:

$$\frac{df_A}{dt} = -f_A(1 - f_A)rc_A(1 - \kappa N) \quad \text{(A2)}$$

This equation shows that, in a well-mixed environment, altruistic suicide is never selected for. At best, when there is no cost of altruistic suicide, the evolution of this trait is neutral. When altruistic suicide is costly, the frequency of altruists decreases.

2. Spatial model

In order to model bacteria-phage dynamics in space, we consider a lattice of a large number of n sites, where each site i can be either empty (o) or occupied by a susceptible (S), an altruistic (A) or a resistant (R) bacteria. S_i, A_i and R_i are indicator functions for the presence of a susceptible, an altruistic or a resistant bacteria, respectively, in site i (e.g. $S_i = 1$ if site i contains a susceptible bacteria, and 0 otherwise). The quantities $p_S = \sum_{i=1}^{n} S_i/n$, $p_A = \sum_{i=1}^{n} A_i/n$ and $p_R = \sum_{i=1}^{n} R_i/n$ measure the proportion of sites of the lattice occupied by a susceptible, an altruistic or a resistant bacterium, respectively. Note that $p_o = 1 - p_S - p_A - p_R$ is the proportion of empty sites in the lattice.

We couple this model of bacteria dynamics with a metapopulation model for virus dynamics. The density of virus on site i is v_i. The quantities $v_S = \sum_{i=1}^{n} v_i S_i/(np_S)$, $v_A = \sum_{i=1}^{n} v_i A_i/(np_A)$ and $v_R = \sum_{i=1}^{n} v_i R_i/(np_R)$ are the average densities of viruses in a site occupied by a susceptible, an altruistic or a resistant bacterium, respectively.

Susceptible, altruistic and resistant bacteria can reproduce into an empty site at rates r, $r(1 - c_A)$ and $r(1 - c_R)$ respectively, and die at rate d. Bacteria in sites containing viruses can become infected at rate ab, where a is the adsorption rate and b is the probability that a virus enters the cell. Upon infection, sensitive bacteria die and liberate free viruses, with burst size B. Altruistic bacteria undergo

the same fate (they are killed by the virus) but do not liberate any virus. Resistant bacteria, in contrast, are not killed after being exposed to the virus.

This gives us the following dynamics for the sensitive and resistant bacteria:

$$\begin{aligned}\frac{dp_S}{dt} &= \left(rq_{o/S}p_S - dp_S - abv_S\right)p_S = \lambda_S p_S \\ \frac{dp_A}{dt} &= \left(r(1-c_A)q_{o/A} - d - abv_A\right)p_A = \lambda_A p_A \\ \frac{dp_R}{dt} &= \left(r(1-c_R)q_{o/R} - d\right)p_R = \lambda_R p_R\end{aligned} \tag{A3}$$

where $q_{o/S}$ (resp. $q_{o/A}$ and $q_{o/R}$) measures the average proportion of empty sites in the neighbourhood of a susceptible (resp. altruistic and resistant) bacteria. Mixing may occur at rates m_B m_V for the bacteria and the viruses, respectively (the following section details how we implement mixing in the simulations). Note that mixing affects the spatial distribution of individuals but does not affect the global densities of bacteria and viruses.

This yields the following equation for the dynamics of the frequency of altruistic suicide strains:

$$\begin{aligned}\frac{df_A}{dt} &= f_A(1-f_A)\lambda_A - f_A f_S \lambda_S - f_A f_R \lambda_R \\ \frac{df_R}{dt} &= f_R(1-f_R)\lambda_R - f_R f_S \lambda_S - f_R f_A \lambda_A\end{aligned} \tag{A4}$$

In the special case where $f_R = 0$ we recover equation (3), given in the main text. In a well-mixed population $q_{o/S} = q_{o/A} = p_o$, and $v_S = v_A$, so the equation simplifies to (see also equation 2 in the main text):

$$\frac{df_A}{dt} = f_A(1-f_A)[-c_A r p_o + abv_A] \tag{A5}$$

In a spatially structured population, $v_S - v_A$ is not necessarily zero, because v_S and v_A depend on mixing and on the dynamics of free viruses.

The equations above can be coupled with a metapopulation model for the dynamics of viruses, as follows. The density v_i of viruses in site i can change as a result of the following processes: decay (at rate d_V), mixing at a rate m_V, adsorption to a bacteria at a rate a or lysis of a sensitive bacteria (and reproduction of the virus) in site i. Reproduction of the virus can only take place upon contact of a bacteria with free viruses in site i. This gives the following differential equation:

$$\frac{dv_i}{dt} = abBv_i S_i - d_V v_i - av_i(S_i + A_i + R_i) + m_V V/n - m_V v_i \tag{A6}$$

where $V = \sum_{i=1}^{n} v_i$ is the global density of viruses. Summing over all the sites on the lattice, we obtain the following equation for the dynamics of the global density of free viruses (see also equation 1 in the main text):

$$\frac{dV}{dt} = abBnv_S p_S - d_V V - an(p_S v_S + p_A v_A + p_R v_R) \quad \text{(A7)}$$

Of course, v_S, v_A and v_R depend on the interplay between virus and bacteria dynamics and are therefore difficult to compute analytically. This is why we use stochastic simulations to investigate the consequences of mixing on the change in frequency of resistance.

3. **Simulations**

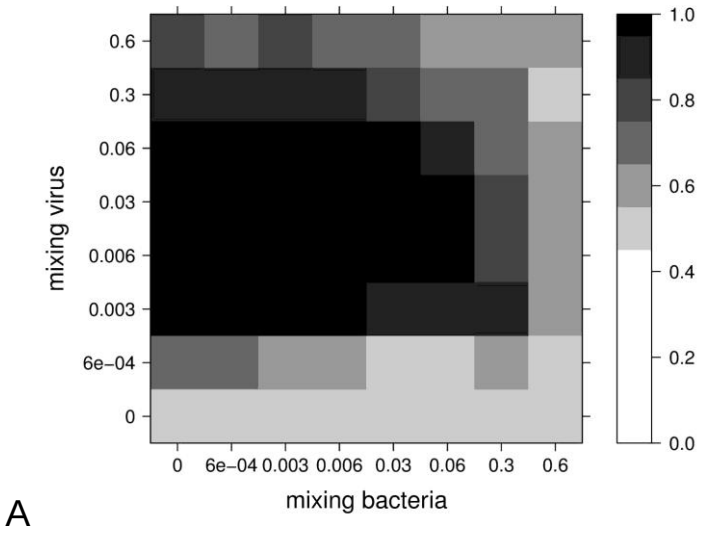
In our simulations, we implement mixing as a process that mimics the disturbance created by the beads in our experiments. Specifically, when a bead lands on a site, the site undergoes a mixing process: the viruses in the site are scattered randomly across all sites in the lattice, while the bacterium is moved to a random empty site. We varied the mixing rates m_B and m_V in our simulations to mimic the different mixing treatments used in our experiments.

In figure 2 the fitness of *Lit* is measured as the ratio between the final and the initial value of $f_A/(1-f_A)$, where f_A refers to the frequency of *Lit* in the host population (i.e. $f_A = p_A/(p_S + p_A + p_R)$). The simulation starts with the following initial conditions: $p_R + p_S = 0.01$ and $f_A = 0.5$. Viruses are introduced at a time $t = 3$ in 25 regularly spaced sites in the lattice. The initial frequency is calculated just after the virus has been introduced. The final frequency is calculated at the end of the simulation ($t = 250$) or just before host extinction if the host population goes extinct. For each mixing treatment we show the mean ± $CI_{95\%}$ of 40 independent simulation runs. Other parameter values used in Figure 2: $r = 1.7$, $d = 0.05$, $c_A = 0.1$, $B = 100$, $d_V = 10^{-7}$, $a = 1$, $b = 0.05$, $n = 100 \times 100$.

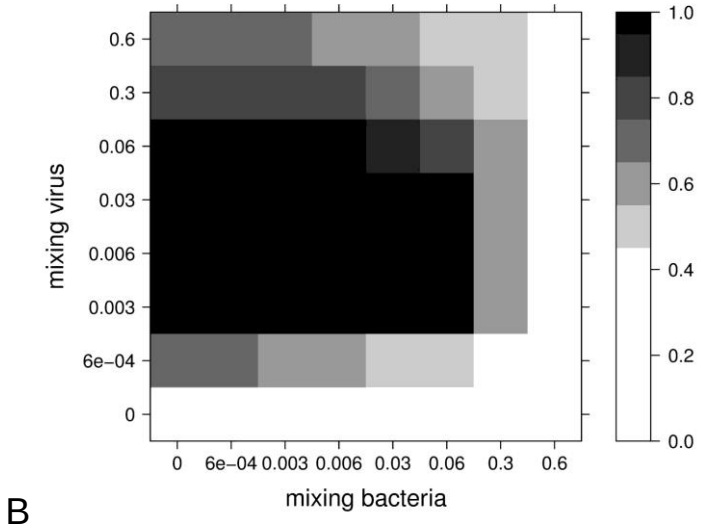
Decoupling bacterium and virus mixing rates: In the main text we focus on the situation where bacteria and viruses have the same mixing rates (i.e., $m_B = m_V$), but we explore the effects of independent mixing rates in Figure S1. More mixing of the bacteria always yields lower selection for the *A* strain because host mixing reduces the genetic structure in the host population. In contrast, mixing of the virus has a non-monotonous effect. No virus mixing prevents the spread of the epidemics, but too much virus mixing removes the difference in the rate of exposition of the two types of hosts. We thus recover the result that only intermediate levels of virus mixing maximize selection for altruistic suicide. This expands the exploration of the effect of mixing presented in Figure 2 and confirms the importance of epidemiological feedbacks on the evolution of altruistic suicide.

Evolution of classical resistance: To study the effect of classical resistance on the evolution of altruistic suicide we allowed both *S* and *A* bacteria strains to mutate at a rate μ towards classical resistance. In Figure S2 we plot the fitness of altruistic suicide against mixing rates (as in Figure 2) for various mutation rates μ. We assumed the costs of altruistic suicide and classical resistance to be equal: $c_A = c_R = 0.1$.

Figure S1: Final frequency of altruistic suicide for increasing values of the costs of altruistic suicide and classical resistance: (A) $c_A = c_R = 0.01$, (B) $c_A = c_R = 0.05$, (C) $c_A = c_R = 0.1$. In each subfigure, the final frequency of altruistic bacteria is shown (as the average over 40 runs) for different combinations of the bacterial and viral mixing rates (m_B, m_V). Other parameter values as in Figure 2.



A



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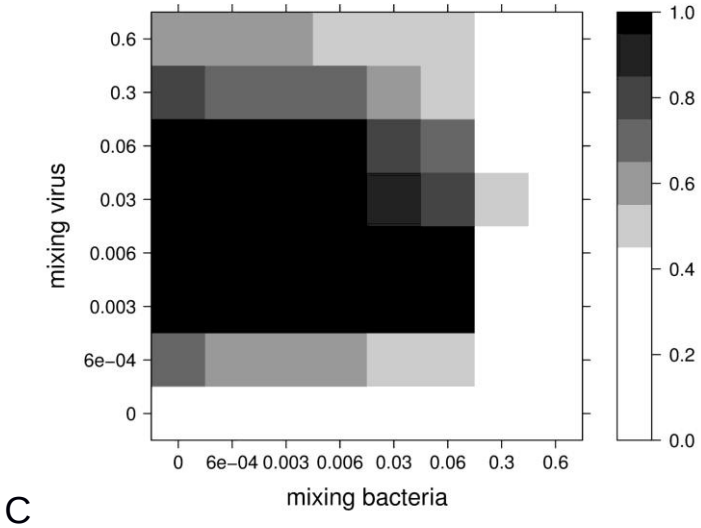

C

Figure S2: Fitness of altruistic suicide for various mutation rate μ towards classical resistance. Parameter values as in Figure 2. The average over 40 runs is shown for different values of the bacteria and virus mixing rates ($m_B = m_V$).