Adaptive Dynamics Course
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Evolution of resistance in host-pathogen systems

In this project, we consider a pathogen that causes lifelong infection of its hosts, and assume that hosts may develop resistance against this pathogen (i.e., are able to defend against getting infected) but only at some cost. The question is how much resistance the host should evolve.

> The following background will hopefully further motivate this project but its understanding is not necessary for the immediate job. From basic models of epidemiology, such as the SIR model, you may be aware of the phenomenon of herd immunity. Herd immunity means that if a large enough fraction of the population is resistant or immune to the pathogen, then there is no epidemic outbreak, because the expected number of secondary infections during the lifetime of a primary infection (i.e. till recovery or death of the infected host) is less than 1 and is thus not enough to replace the primary infected host. The point here is that not every individual need to be resistant for herd immunity, and it is possible to enjoy protection from herd immunity without being resistant to the disease. When resistance is costly, there is an incentive to rely on herd immunity and avoid paying the cost. This is a form of cheating, because such non-resistant individuals enjoy benefit from others' costly resistance. Of course if non-resistant cheaters are too frequent, then herd immunity collapses. Yet we may expect the evolution of resistant and cheating strategies, and this is what the present project will elaborate on.

A basic ecological model of a lifelong infection is given by

$$\begin{aligned} \frac{dS}{dt} &= r(\beta)\cdot(S+I) - q(S+I)S - \beta SI \\ \frac{dI}{dt} &= \beta SI - \alpha I - q(S+I)I \end{aligned} \qquad (1)$$

where S and I are respectively the number of susceptible and the number of infected hosts. It is assumed that susceptible and infected individuals reproduce equally and newborns are free of infection, hence all the $r\cdot(S+I)$ newborns are added to the susceptibles (r is the birth rate). The death rate, $q(S+I)$, depends linearly on total population size $S+I$ such that in absence of the pathogen, the host population grows according to the logistic model. β is the infection rate and α is the rate of death caused by the disease, called the virulence.

We assume that different strains of the host differ in how much they are resistant to the disease. More resistance implies a lower rate of contracting the disease and therefore a smaller value of β (full resistance is achieved when $\beta = 0$). Resistance implies a cost: we assume that more resistant strains have lower birth rates such that r is some increasing function $r(\beta)$ in equations (1).

Assume that a rare mutant host strain characterised by β_{mut} is present in the established population of strain β. The population dynamics of the mutant strain are given by

$$\begin{aligned}\frac{dS_{mut}}{dt} &= r(\beta_{mut})\cdot(S_{mut}+I_{mut}) - q\left(S+I\right)S_{mut} - \beta_{mut}IS_{mut}\\ \frac{dI_{mut}}{dt} &= \beta_{mut}IS_{mut} - \alpha I_{mut} - q\left(S+I\right)I_{mut}\end{aligned} \tag{2}$$

where *S* and *I* are the equilibrium densities of the resident population calculated from equation (1).

Whether or not the mutant can invade can be determined by investigating the stability of the trivial equilibrium of eqs. (2), $S_{mut}=0, I_{mut}=0$: If the trivial equilibrium is unstable then mutants grow from a low population density. This can be done calculating the Jacobian of eqs. (2). There is however a simpler way to obtain a fitness proxy: Calculate the number of newborn offspring expected by a mutant host during its lifetime (the basic reproduction number, R_0). If R_0 is greater than 1, then the mutant strain spreads, otherwise the mutant dies out. One can use R_0 to obtain PIPs, singular strategies, and their stability properties just as one can use the invasion fitness.

To calculate R_0 of the mutant strain, notice first that every individual starts its life uninfected. The uninfected stage is left either via infection, which occurs at rate $\beta_{mut}I$, or via death, which occurs at rate $q(S+I)$. Because *S* and *I* of the resident population are constant at equilibrium, both infection and death are exponential decay processes. The rate of removal of susceptibles is $\beta_{mut}I+q(S+I)$ and therefore the expected lifetime spent uninfected is $1/\left[\beta_{mut}I+q(S+I)\right]$. Uninfected lifetime ends with infection rather than death with probability $\beta_{mut}I/\left[\beta_{mut}I+q(S+I)\right]$. If the individual gets infected but remains alive, it can expect an additional lifespan of $1/\left[\alpha+q(S+I)\right]$ as infected (note once somebody is infected, it stays infected till death; the formula is analogous to the uninfected lifespan except that disease-induced mortality replaces infection). If, on the other hand, an individual exits the uninfected stage via death, there is no lifetime to add. Putting this together, a newborn can on average expect a lifetime of

$$L_{mut} = \frac{1}{\beta_{mut}I+q(S+I)} + \frac{\beta_{mut}I}{\beta_{mut}I+q(S+I)}\cdot\frac{1}{\alpha+q(S+I)} \tag{3}$$

(note that this depends both on the mutant and on the resident trait values β_{mut} and β; the latter is via the equilibrium densities *S* and *I*). The individual gives birth to $r(\beta_{mut})$ offspring per unit of time throughout its lifetime, hence the total number of offspring of a mutant is

$$R_0 = r(\beta_{mut})L_{mut} \tag{4}$$

When necessary for numerical work, assume the trade-off function $r(\beta)$ is either linear [$r(\beta) = a\beta + c$] or is given by

$$r(\beta) = c - \frac{1}{a(\beta - b)} \tag{5}$$

assuming $a > 0$. You can use the left branch of this hyperbola (with $b > 0, c > 0$ and $\beta < b$) for a convex trade-off function or the right branch (with $b < 0, c > 0$) for a concave trade-off function.

Investigate the adaptive dynamics of β by constructing PIPs and exploring the stability properties of monomorphic singularities. Find examples for evolutionary branching. Construct the isocline plot for an example with evolutionary branching to explore the coevolution of two host strains: Will one strain evolve to be a cheater? Investigate the effect of changing the virulence (α) on the adaptive dynamics.