Inducible defence and the social evolution of herd immunity

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Many organisms vary their level of investment in defensive characters. Protective traits may be induced upon exposure to predators or parasites. In a similar way, humans vaccinate in response to threatening epidemics. When most group members defend themselves, epidemics die out quickly because parasites cannot spread. A high level of group (herd) immunity is therefore beneficial to the group. There is, however, a well-known divergence between the optimum degree of induction for selfish individuals and the level of induction that maximizes group benefit.

I develop two optimality models for the frequency of induction. The first model shows that higher relatedness favours more induction and a smaller difference between selfish and cooperative optima. The second model assumes variation in the vigour of individuals and therefore differences in the relative cost for induction. The model predicts that strong individuals induce more easily than weak individuals. Small differences in vigour cause a large divergence in the optimal levels of induction for strong and weak individuals.

The concept of genetic relatedness in an evolutionary model is analogous to correlated interests and correlated strategies in an economic model of human behaviour. The evolutionary models presented here therefore provide a basis for further study of human vaccination.

Keywords: disease resistance; vaccination; host–parasite; predator–prey; herbivory

1. INTRODUCTION

Cladocerans develop protective helmets when predators threaten (Havel 1987). Plants induce a variety of structural and biochemical defences in response to herbivory or infection (Karban & Baldwin 1997). Humans engender immunity by vaccination. These inducible defences have two widely discussed features: protection against attack, and costs that prevent constant expression by all members of a population (Harvell 1990).

The frequency of defended individuals in a group influences the dynamics of attack and disease (Anderson & May 1991). When most group members defend themselves, epidemics die out quickly because parasites cannot spread. Similarly, predators and herbivores may abandon well-defended, unprofitable groups. The phrase 'herd immunity' summarizes the ways in which the frequency of resistance influences the dynamics of attack (Anderson & May 1990).

The optimum induction strategy for an individual depends on the probability of attack and the costs of defence (van Baalen 1998). At some frequency of group immunity, individual hosts no longer gain sufficient benefit to outweigh the cost of induction. That optimum, based on a game-theory analysis of costs and benefits to selfish individuals, is often well below the frequency of immunity that provides optimum protection per individual in a cooperative group (Anderson & May 1990). Such tensions between the optimum for selfish individuals and the optimum for members of a cooperative group are common in social interactions (Frank 1998).

I develop two simple optimality models for the frequency of induction favoured by natural selection. The first model shows the influence of genetic relatedness among group members on the frequency of induction. As expected, higher relatedness favours more induction and a smaller difference between selfish and cooperative optima.

The second model assumes variation in the vigour of individuals and therefore differences in the relative cost for induction. The model predicts that vigorous individuals induce more easily. Relatively strong and weak individuals diverge in optimal phenotype very quickly as the difference between their levels of vigour increases. Surprisingly, the smaller the cost of induction, the more rapid the differentiation between strong and weak.

2. RELATEDNESS

Individuals that induce defence pay a cost in reduced fitness and gain protection against attack. The probability of attack declines as the average frequency of induction in the group rises. The following model captures these features:

$$w(y,z) = (1 - cy)[1 - a(1 - y)f(z)],$$

where the fitness of an individual, w, depends on its probability, y, of inducing defence in response to a signal,

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and the average probability, z, of induction over all members of the group. Here y and z are assumed to be measures of additive genotypic value (breeding value) under the standard assumption that the slope of phenotype on breeding value is one. The cost of induction is c and the probability of future attack is a. The term $1-y$ describes protection from attack for those who induce defences, and $f(z)$ is a decreasing function of z that summarizes the reduction in attack probability from increasing herd immunity. Frank (1998) explains this type of formulation and the following approach.

The optimum probability of induction, y^*, is obtained by maximization of w with respect to small variants in y, from the solution of

$$\frac{\mathrm{d}w}{\mathrm{d}y} = \frac{\partial w}{\partial y} + r\frac{\partial w}{\partial z} = 0,$$

evaluated at $y = z = y^*$. The partial derivatives arise from standard application of the chain rule for differentiation, and $r = \mathrm{d}z/\mathrm{d}y$ is the coefficient of relatedness from kin-selection theory (Taylor & Frank 1996). Note that this coefficient is simply the slope of group genotype on individual genotype or, equivalently, the slope of the average social partner's genotype on the actor's genotype.

The first term of the derivative is

$$\frac{\partial w}{\partial y} = a(1-cy^*)f(y^*) - c[1 - a(1-y^*)f(y^*)],$$

which is the direct, marginal effect of induction on the individual's own fitness. The second term is

$$r\frac{\partial w}{\partial z} = -ra(1-cy^*)(1-y^*)f'(y^*),$$

which is the marginal effect of induction on neighbours' fitness, weighted by the coefficient of relatedness, r. Here f' is the partial derivative of f with respect to z. The two partial derivatives of w are the cost and benefit in a marginal form of Hamilton's rule for kin selection (Hamilton 1964; Frank 1998).

These terms provide some clues about marginal costs and benefits. Solution requires an explicit assumption about the form of the herd immunity function, f. For simplicity, let $f(z) = 1 - z$, that is, $f'(z) = -1$, and thus susceptibility declines linearly with the frequency of defended individuals in the group. More realistic functions, derived from explicit dynamic considerations, are possible, but the purpose here is simply to illustrate the processes that shape induction.

The linear assumption for herd immunity yields a quadratic

$$acx^2(2+r) + x(1-c)a(1+r) - c = 0, \qquad (1)$$

where $x = 1 - y^*$. This is easily solved by standard methods, but the solution has many terms and must be plotted to gain some insight (figure 1).

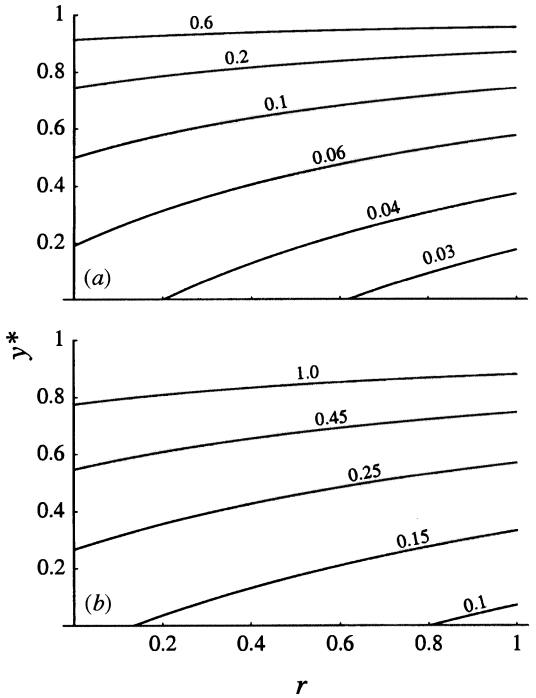

Figure 1. The equilibrium probability of induction when neighbouring members of a herd include relatives. Plots show solutions of equation (1) for the parameters: c, cost of resistance, ($(a)c = 0.05$; $(b)c = 0.2$) r, relatedness among group members who are connected by a strong influence on each other's ultimate probability of exposure to attack; and a, the probability of attack or infection of a group member. The values of a are shown above each curve. The probability of attack may be thought of as a conditional probability of future attack given a prior history of exposure to enemies.

3. VARIABLE RESOURCES

Individuals typically differ in the amount of resources available to them and in their overall vigour. Induction of defence may require a smaller proportion of total resources from relatively stronger individuals. I present a model in which individuals differ in vigour and there is no relatedness among group members ($r = 0$). For individuals with vigour or resource level k, fitness is

$$w_k = (k - cy_k)[1 - a(1-y_k)F],$$

where y_k is the probability of induction for resource level k. The herd immunity function, F, depends on the values, y_k, for all resource levels, k, and on the probability distribution for k. A local optimum is obtained by simultaneous solution of $\mathrm{d}w_k/\mathrm{d}y_k = 0$ for all k, which yields

$$y_k^* = \begin{cases} 0 & x_k < 0 \\ 1 & x_k > 1, \\ x_k & \text{otherwise} \end{cases}$$

where

$$x_k = \frac{akF - c(1-aF)}{2acF}. \qquad (2)$$

The herd immunity function, F, depends on the values of y_k; thus explicit assumptions for F are required for the solution. As before, assume that F declines linearly with the average level of induction in the group, $F = 1 - \bar{y}$. (The overbar denotes population average; in this model there is no distinction between group and population averages.) The solution can now be obtained if we also assume that $0 \leqslant x_k \leqslant 1$ for all k, implying that x_k and y_k

are equivalent. I make this assumption for the remainder of this section. I also assume that the average resource level is one ($\bar{k} = 1$).

Next, note that when one integrates the left and right sides of equation (2) over the distribution of k, one obtains

$$1 - F = \frac{aF - c(1 - aF)}{2acF}.$$

Replacing F with $1 - \bar{y}$ according to the definition given above, the optimum average probability of induction $\bar{y}^*$ can be obtained. The solution is identical to that of the previous section for y^*, in which there was no variation in resources and $r = 0$. Thus the average level of induction is not influenced by variation in resources when $0 < x_k < 1$ for all k. A few substitutions show that the optimum probability of induction for each resource level is

$$y_k^* = \bar{y}^* + \frac{k - \bar{k}}{2c}.$$

If costs of induction are relatively small, then small variations in vigour, k, cause a large divergence in the optimum probability of induction between strong (high k) and weak (low k) individuals. As the cost, c, declines, the divergence in behaviour between strong and weak individuals rises.

4. CONCLUSIONS

The models make two predictions. First, selection favours members of kin groups to invest more in defence than individuals that mix primarily with non-relatives. This could, for example, be tested within a bird population by comparing the immune-system responsiveness of individuals that live in cooperative family groups with the responsiveness of those that were floating as unattached individuals. There is, of course, the difficulty of many uncontrollable factors in wild populations; manipulative experiments in natural populations or in captive colonies may be necessary.

The second prediction concerns the rapid change of induction status favoured with changes in vigour. This could be tested most easily by manipulating food supply. Small organisms such as *Daphnia* should be relatively easy to study in this way, but the same ideas apply to inducible defences of all species.

The discrepancy between individual and group optima is an important public health issue in human vaccination. The models developed here depend on evolutionary optimization of fitness, but the concepts could be developed within an economic context of maximizing some objective function (Maynard Smith 1982). Because the goal in both evolutionary and economic terms is efficiently to avoid attack, the outcomes should be similar.

The models here highlight that relatedness reduces the gap between individual and group optima. Relatedness can be interpreted as correlated economic interests and correlated behavioural strategies among group members (Frank 1998). Thus the role of population structure in the public health problem can be studied with methods that are similar to those developed here.

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REFERENCES

Anderson, R. M. & May, R. M. 1990 Modern vaccines: immunisation and herd immunity. *Lancet* **335**, 641–645.

Anderson, R. M. & May, R. M. 1991 *Infectious diseases of humans: dynamics and control.* Oxford University Press.

Frank, S. A. 1998 *Foundations of social evolution.* Princeton University Press.

Hamilton, W. D. 1964 The genetical evolution of social behaviour. I, II. *J. Theor. Biol.* **7**, 1–16, 17–52.

Harvell, C. D. 1990 The ecology and evolution of inducible defenses. *Q. Rev. Biol.* **65**, 323–340.

Havel, J. 1987 Predator-induced defenses: a review. In *Predation: direct and indirect impacts on aquatic communities* (ed. W. C. Kerfoot & A. Sih), pp. 263–278. Hanover, New Hampshire: University Press of New England.

Karban, R. & Baldwin, I. T. 1997 *Induced responses to herbivory.* University of Chicago Press.

Maynard Smith, J. 1982 *Evolution and the theory of games.* Cambridge University Press.

Taylor, P. D. & Frank, S. A. 1996 How to make a kin selection model. *J. Theor. Biol.* **180**, 27–37.

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