

Linear Models Are Inappropriate to Estimate Relative Parasitic Fitness of Pathogens in Heterogeneous Host Populations

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Sun and Zeng (7) present a method of estimating the relative fitness of asexual pathogens growing in cultivar mixtures. They suggest using a linear combination of fitnesses of a set of genotypes ("races") on several cultivars, weighted by the proportion of each cultivar in the mixture. They define fitness over the season, f , as the ratio of genotype frequencies at the end and beginning of the season. Thus, for a population of two genotypes at frequency p_1 and p_2 , with a second subscript, 0, denoting the beginning of the season, the relative fitness of genotype 1 to genotype 2 is

$$f_{12} = (p_1/p_2)/(p_{10}/p_{20}) \quad (1)$$

(equation 2 in Sun and Zeng [7]).

This definition can be justified mathematically as follows. If v_i is the absolute fitness (number of spores produced per spore present at the beginning of the season) of genotype i , then

$$\begin{aligned} p_1 &= v_1 p_{10} / (v_1 p_{10} + v_2 p_{20}) \\ p_2 &= v_2 p_{20} / (v_1 p_{10} + v_2 p_{20}) \end{aligned} \quad (2)$$

As a result, the fitness of one genotype relative to the other is

$$f_{12} = v_1/v_2 = (p_1/p_2)/(p_{10}/p_{20}) \quad (3)$$

A numerical example may make this clearer. Consider a completely isolated crop: if genotypes 1 and 2 are both inoculated at 100 spores per square meter and by the end of the season 2,000,000 and 1,000,000 spores per square meter, respectively, are produced and released into a spore cloud, the fitness of genotype 1 relative to genotype 2 would be 2 and the fitness of genotype 2 relative to genotype 1 would be 0.5.

Sun and Zeng (7) introduce the notation f_{ijk} to denote fitness of race i relative to race j measured over an entire season on cultivar k . They then propose, without further argument, that where a mixture of cultivars is present, with the k th cultivar occupying a proportion, c_k , of the total, the "overall fitness of the i th race [genotype] relative to the j th race [genotype] can be expressed by the following model:

$$(p_i/p_j)/(p_{i0}/p_{j0}) = c_1 f_{ij1} + c_2 f_{ij2} + \dots + c_m f_{ijm} \quad (4)$$

This expression is wrong, however. To make this clear, we will use a simple extension of the numerical example above. For simplicity we assume that there is no movement of spores from one cultivar to the other (no allo-infection) during the entire season. Imagine that on the other cultivar the absolute fitnesses of genotypes 1 and 2 from the first example are reversed. With a 1:1 mixture of the cultivars at the end of the season, inoculated at the same densities as before and assuming no allo-infection, we would have

a contribution from cultivar 1 of 1,000,000 spores of genotype 1 per square meter and 500,000 spores of genotype 2 per square meter; from cultivar 2 we would have 500,000 spores of genotype 1 per square meter and 1,000,000 spores of genotype 2 per square meter. As a result, in the spore cloud we have 1,500,000 spores of each genotype per square meter. Neither genotype has increased in frequency, i.e., the overall relative fitness is 1 for both genotypes, but using equation 4, we would obtain a relative fitness of $0.5 \times 2 + 0.5 \times 0.5 = 1.25$ for either genotype relative to the other. This is clearly nonsense.

The mathematics behind the numerical calculations of spore numbers can be expressed more generally by an extension of equations 2. For simplicity we assume only two cultivars are present but that there are n pathogen genotypes. Then, we can calculate the new genotype frequencies in the spore cloud, taking the composition of the host into account. First, we calculate the average number of spores of each genotype produced on two cultivars together per original spore:

$$\bar{v}_i = v_{i1}c_1 + v_{i2}c_2 \quad (5)$$

We average the result over the genotypes to produce a mean fitness. The new frequency of genotype i is obtained by multiplying the initial frequency by \bar{v}_i and dividing by the mean fitness to give

$$\begin{aligned} p_1 &= \frac{\bar{v}_1 p_{10}}{\bar{v}_1 p_{10} + \dots + \bar{v}_i p_{i0} + \dots + \bar{v}_n p_{n0}} \\ &\vdots \\ p_i &= \frac{\bar{v}_i p_{i0}}{\bar{v}_1 p_{10} + \dots + \bar{v}_i p_{i0} + \dots + \bar{v}_n p_{n0}} \\ &\vdots \end{aligned} \quad (6)$$

This implies that

$$(p_i/p_{i0})/(p_j/p_{j0}) = \bar{v}_i/\bar{v}_j \quad (7)$$

Equation 7 can be rewritten as

$$(p_i/p_{i0})/(p_j/p_{j0}) = c_1 f_{ij1} \frac{v_{j1}}{\bar{v}_j} + c_2 f_{ij2} \frac{v_{j2}}{\bar{v}_j} \quad (8)$$

Comparing equation 8 with equation 4, it is obvious that even in the simplest case with no allo-infection equation 4 is valid only if each genotype has identical fitness on all cultivars. Then, the way to estimate relative fitnesses is both simple and well known (3,5).

For most pathogens it is extremely unlikely that within a cultivar mixture no allo-infection will occur during a season. An alternative crude model for the entire season would result if the aerial spore cloud was completely randomly mixed at the end of each generation, with contributions of spores from each cultivar

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proportional to its area. This is probably no more realistic for real mixtures than an assumption of no allo-infection, but it provides an extreme alternative. In this case, with v now denoting absolute fitness per generation, if there were t generations in the season

$$(p_i/p_{i0})(p_j/p_{j0}) = \frac{(v_{i1}c_1 + v_{i2}c_2)^t}{(v_{j1}c_1 + v_{j2}c_2)^t} \quad (9)$$

Equation 9 cannot be manipulated into a form compatible with equation 4 and would not even be linear in cultivar proportions. More realistic models require even more complicated calculations (1,4,6).

Our results unfortunately indicate that Sun and Zeng's (7) otherwise elegant estimation procedure is incorrect, because it depends on the linearity of equation 4. Statistical analysis of changes according to the model embodied in equation 6 may need explicit likelihood- or resampling-based methods because of the intrinsically nonlinear nature of the equations.

An example of how models of genotype-frequency dynamics due to differences in crop area may be used is provided by Hovmøller et al. (2) and Østergård and Hovmøller (6). These authors used knowledge of the relative frequency of crops carrying different combinations of resistance genes to *Erysiphe gram-*

inis f. sp. *hordei* to predict associations between virulence genes and changes in frequency of virulence alleles in the aerial population of spores.

In conclusion, we emphasize that any use of Sun and Zeng's (7) procedure will result in inconsistent and meaningless estimates.

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