Electronic Supplementary Material for

An inclusive fitness analysis of synergistic interactions in structured populations

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ESM-A The linearity of $R_{X \rightarrow YZ}$

We begin in an infinite population and show that the relatedness coefficient $R_{X \rightarrow YZ} = \frac{\text{cov}(x, yz)}{\text{cov}(x, x)}$ is linear in the overall population allele frequency $p$. There are a number of ways to do this but here we make use of the concept of identity by descent (IBD). We say that two genes are IBD if they have a common ancestor where we make the assumption that a gene that migrates a long distance will never meet a common ancestor. We begin with the numerator of $R_{X \rightarrow YZ}$. Write

\[ \text{cov}(x, yz) = \text{E}(xyz) - \text{E}(x)\text{E}(yz). \]  \hspace{1cm} (A1)

The first term $\text{E}(xyz)$ is simply the probability that $X$, $Y$ and $Z$ are all $A$ and this will be

- $p$ if all three individuals are IBD at the locus in question,
- $p^2$ if only two of the three are IBD, and
- $p^3$ if none of the three are IBD

Thus $\text{E}(xyz)$ is a linear combination of $p, p^2$ and $p^3$ so is a polynomial of degree at most 3 (and at least 1). By a similar argument, $\text{E}(xy)$ is a polynomial of degree 1 or 2, and since $\text{E}(x) = p$, $\text{cov}(x, yz)$ is a polynomial of degree 2 or 3. Note now that if $p = 0$ or 1, $\text{cov}(x, yz)$ will equal zero, and thus $\text{cov}(x, yz)$ must be divisible by $p(1-p)$. It follows that $\text{cov}(x, yz)$ has the form $p(1-p)(s+rp)$ for parameters $s$ and $r$ that are independent of $p$. Finally, $\text{cov}(x, x) = \text{var}(x) = p(1-p)$ in a haploid population, so that the quotient $R_{X \rightarrow YZ}$ must have the form $s+rp$.

An interesting simple example of this is found in an infinite population, when one of $Y$ and $Z$ is actually $X$. We have:

\[ \text{cov}(x, xy) = \text{E}(x^2 y) - \text{E}(x)\text{E}(xy) = \text{E}(xy) - \text{E}(x)\text{E}(xy) \]
\[ = (1-p)\text{E}(xy) = (1-p)[\text{E}(x)\text{E}(y) + \text{cov}(x, y)] \]
\[ = (1-p)[p^2 + p(1-p)R_{X \rightarrow Y}] = p(1-p)[p + (1-p)R_{X \rightarrow Y}] \]

Hence: $R_{X \rightarrow XY} = \frac{\text{cov}(x, xy)}{\text{cov}(x, x)} = p + (1-p)R_{X \rightarrow Y}$.

The argument in a finite population is parallel but technically more complex and a comment on this is found at the end of ESM-D.

Here we use an inclusive-fitness framework to import the elegant argument of Tarnita et al (2009) into an infinite population with long-range migration at a particular allele frequency $p$.

Tarnita et al (2009) begin by showing that the condition for allele A to be favoured over B has the form

$$k_1a + k_2b > k_3c + k_4d$$

where the $k_i$ are independent of the payoffs but do depend on the population structure, the update rule (how old breeders are replaced by new), the mutation rate and the population size. Our analogue of eq. (B1) comes by writing eq. (2.6) for the inclusive-fitness effect of A in the form:

$$W_{IF-A} = k_1(p)a + k_2(p)b - k_3(p)c - k_4(p)d$$  \hspace{1cm} (B2)

Unlike Tarnita et al (2009), we need to explicitly display the dependence of the $k_i$ on the equilibrium allele frequency $p$, but we emphasize that they are independent of the payoffs, as the covariances in eq. (2.6) are calculated in the neutral population (Taylor et. al 2007). The same is true of other aspects of the Tarnita et al (2009) argument that depend on the A-B symmetry, and essentially for the same reason, that the components of the inclusive fitness effect are covariances and they are calculated in the neutral population in which A and B have the same effect.

Following the Tarnita et al (2009) argument, we observe that the inclusive-fitness effect of B must be the analogue of (B2) with the payoffs suitably permuted and $p$ replaced by $q = 1-p$:

$$W_{IF-B} = k_1(q)d + k_2(q)c - k_3(q)b - k_4(q)a$$

$$= -k_4(q)a - k_3(q)b + k_2(q)c + k_1(q)d$$  \hspace{1cm} (B3)

Since the inclusive-fitness effect of an allele is proportional to its initial (when the switch is turned on) rate of increase in frequency (Taylor et. al 2007, eq. 3.6):

$$W_{IF-B} = -\lambda W_{IF-A}$$

for some $\lambda > 0$, and hence, from (B2) and (B3):

$$k_4(q) = \lambda k_1(p), \quad k_3(q) = \lambda k_2(p), \quad k_2(q) = \lambda k_3(p) \quad \text{and} \quad k_1(q) = \lambda k_4(p).$$

Thus

$$k_4(q) = \lambda k_1(p) = \lambda^2 k_3(q).$$

It follows that $\lambda^2 = 1$, and since $\lambda > 0$, $\lambda = 1$. Thus

$$k_4(q) = k_1(p) \quad \text{and} \quad k_3(q) = k_2(p)$$

and eq. (B2) can be written:

$$W_{IF-A} = k_1(p)a + k_2(p)b - k_3(q)c - k_1(q)d.$$  \hspace{1cm} (B4)
Now using the payoff matrix:

\[
\begin{bmatrix}
a & b \\
c & d
\end{bmatrix}
= \begin{bmatrix}
B - C + D & -C \\
B & 0
\end{bmatrix},
\]

(B4) becomes:

\[
W_{IF-A} = [k_1(p) - k_2(q)]B - [k_1(p) + k_2(p)]C + k_1(p)D
\]  

(B5)

Using the fact that in the absence of synergy \((D=0)\), \(W_{IF}\) involves only the standard relatedness coefficients \(R_{X\rightarrow Y}\) (Queller 1985), we write eq. (B5) as

\[
W_{IF-A} = \beta B - \gamma C + k_1(p)D
\]  

(B6)

where \(\beta\) and \(\gamma\) are independent of \(p\). A comparison of eqs. (B5) and (B6) allows us to write:

\[
k_1(p) = \frac{\beta + \gamma}{2} + \frac{k_2(p) - k_3(p)}{2}.
\]  

(B7)

The last term on the right is linear in \(p\) (ESM-A) and is zero when \(p = \frac{1}{2}\), and so it must have the form \((p - \frac{1}{2})\alpha\) where \(\alpha\) is independent of \(p\) and this gives us the form of eq. (3.5).

ESM-C. The \(p - \frac{1}{2}\) term in eq. (3.5) is first order in the long-term migration rate.

To make this argument, we refer to a couple of equations in ESM-B. Note that the off-diagonal entries \(b\) and \(c\) in the payoff matrix can contribute to an individual’s fitness only when both alleles are present in the focal neighbourhood. When long-range migration is rare, local neighbourhoods will tend towards homozygosity, and must await a migration event for heterozygosity to be restored. It follows from eq. (B2) that the coefficients \(k_2(p)\) and \(k_3(p)\) of \(b\) and \(c\) will be (at least) first order in the long-range migration rate. It then follows from eq. (B7) that this will be the case for the difference between \(k_1(p)\) and \((\beta + \gamma)/2\), and hence from eq. (B5) it will also hold for \(\alpha\).

We remark that this argument can be just as easily made for a finite population. In this case, for the entries \(b\) and \(c\) to appear in the calculation both alleles must be present in the population and as a mutation is necessary to free the population from fixation, the relative amount of time the population will be unfixed, and hence the coefficients \(b\) and \(c\), will be first order in the mutation rate.
ESM-D. Allele-frequency change in a finite population.

By the state of the population, we will mean the specification of the A-B configuration among the nodes, with isomorphic configurations generally identified. A finite population does not have an equilibrium state in the same way as an infinite population and, certainly when the population is small, random sampling of genes will cause the population allele frequency $\bar{x}$ to drift and fixation will inevitably occur. At this point we need mutation to unfix the population and restart what becomes a continual drift-fixation-mutation cycle. Selection, of course, can only act in the unfixed states and Price's (1970) equation (3) will then give the selective component of allele-frequency change. But of course what it gives us will depend very much on the state of the population.

Our measure of overall allele-frequency change will be an average of the change given by eq. (2.3) where each population state is weighted by its long-term average neutral frequency of occurrence. (Rousset and Billiard 2000, Taylor et. al. 2007). We write this as:

$$E \left[ \frac{dE(x)}{dt} \right] = E \left[ \text{cov}(x, W_X) \right]$$

(D1)

Here we use round brackets to signal a within-state calculation, and square brackets for a calculation over all states with their long-term frequencies (Taylor et al 2007). Thus the covariance on the right is calculated in each population state and the expectation is taken over all states with their long-term frequency. The inclusive fitness effect is still given as

$$W_{IF} = \sum_i R_i \Delta w_i \text{ (eq. 2.4) but the relatedness and the fitness effects become long-term averages over all states. This leads to the following formula:}$$

$$W_{IF} = \frac{E \left[ \text{cov}(x, W_X) \right]}{E \left[ \text{cov}(x, x) \right]}$$

(D2)

which is the finite-population analogue of eq. (2.5) and the corresponding coefficients of relatedness are the analogue of eq. (2.7):

$$R_{X \rightarrow Y} = \frac{E \left[ \text{cov}(x, y) \right]}{E \left[ \text{cov}(x, x) \right]}, \quad R_{X \rightarrow YZ} = \frac{E \left[ \text{cov}(x, yz) \right]}{E \left[ \text{cov}(x, x) \right]}.$$  

(D3)

To work with $E \left[ \text{cov}(x, \bullet) \right]$ we use the covariance decomposition theorem over all states (Ross 1998): $\text{cov}[x, \bullet] = E \left[ \text{cov}(x, \bullet) \right] + E[E(x), E(\bullet)]$, as it is $\text{cov}[\bullet, \bullet]$ to which the IBD argument of ESM-A can be applied. See Taylor et al (2007) for technical details.
Literature cited


