

Mean curvature versus normality: A comparison of two approximations of Fisher's geometrical model

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Abstract

Fisher's geometrical model amounts to a description of mutation and selection for individuals characterised by a number of quantitative traits. In the present work the fitness landscape is not assumed to be spherically symmetric, hence different points, i.e. phenotypes, on a surface of constant fitness generally have different curvatures. We investigate two different approximations of Fisher's geometrical model that have appeared in the literature. One approximation uses the average curvature of the fitness surface at the parental phenotype. The other approach is based on a normal approximation of a distribution associated with new mutations. Analytical results and simulations are used to compare the accuracy of the two approximations.

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1. Introduction

In his book *The Genetical Theory of Natural Selection*, Fisher (1930) introduced a description of mutation and selection of quantitative traits that was essentially geometrical in content. This has come to be known as Fisher's geometrical model. Individuals were characterised by the value of n quantitative traits. These trait values were taken as the Cartesian coordinates in an n dimensional space of characters and an individual, with their particular set of n characters, was represented as a point in this space.

Fisher was one of the first people to consider fitness to depend on all relevant biological variables, when he allowed selection to depend on the n quantitative traits characterising an individual. Implicit in Fisher's writing, was the existence of a single fitness optimum. Hence for phenotypes in the vicinity of this optimum, selection is of a stabilising type. Phenotypes far from this optimum are subject to directional selection.

The process of mutation results in a mutant offspring being located at a different position in the character space to that of their parent (for simplicity we couch matters in

the language of an asexual population). When the number of characters, n , is large, results from the model confirm the commonly held belief, that most random changes of a complex organism reduce fitness, and that only a small fraction are beneficial (increase fitness). Amongst other things, this model actually allows us to quantify the proportion of mutations that are beneficial and, quite recently, such a model has been considered in a variety of different contexts (Rice, 1990; Hartl and Taubes, 1996, 1998; Peck et al., 1997; Orr, 1998, 1999, 2000, 2006; Burch and Chao, 1999; Poon and Otto, 2000; Barton, 2001; Welch and Waxman, 2003; Whitlock et al., 2003; Waxman and Welch, 2005; Waxman, 2006; Martin and Lenormand, 2006). Indeed this model and generalisations of it are becoming part of the conceptual and theoretical toolkit of workers in the area of evolutionary adaptation.

In the present work, we compare two approaches to approximating Fisher's geometrical model, when the fitness landscape is not spherically symmetric—which is a highly idealised situation—but rather, when a surface of constant fitness has different curvatures at different locations on the surface.

The first approach (Rice, 1990) involved averaging over curvatures. Thus at the location of a parental phenotype, in

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the n dimensional space of characters, an approximate (curvature averaged) fitness surface was used in place of the exact fitness surface. An alternative approach (Waxman and Welch, 2005; Waxman, 2006) approximated the problem as one in which new mutations are associated with a Gaussian random variable that depends on the parental phenotype. It is hard to directly compare the two approximations since they involve related quantities, but in apparently quite different combinations. It is the purpose of the present work to make a comparison of the two approximations. We shall approach this by looking at a specific case that clearly illustrates the differences and has the virtue of being exactly calculable within a well-defined approximation scheme.

2. The basic form of Fisher’s model

The values of the n quantitative characters that describe the relevant phenotype of an individual are $\mathbf{z} = (z_1, z_2, \dots, z_n)$ and each of the different characters, z_i , is taken to range from $-\infty$ to ∞ .

Individuals are assumed to be subject to stabilising selection, with the characters defined in such a way that the optimum of the fitness function lies at the coordinate origin, $\mathbf{z} = (0, 0, \dots, 0)$. In Fisher’s original analysis, the fitness landscape was implicitly taken to be spherically symmetric, with the fitness of an individual depending only on the Euclidean distance of \mathbf{z} from the origin:

$\|\mathbf{z}\| \equiv \sqrt{z_1^2 + z_2^2 + \dots + z_n^2}$, for example $\exp(-\sigma\|\mathbf{z}\|^2)$ where σ is a positive constant whose value is a measure of the strength of stabilising selection. A consequence of spherical symmetry is that surfaces of constant fitness are hyperspheres centred on the coordinate origin, that is, circles if $n = 2$, spheres if $n = 3$ and higher dimensional analogues of these for higher n .

The change in characters, due to mutation, is given by n random mutational changes on the different characters, namely the numbers $\mathbf{r} = (r_1, r_2, \dots, r_n)$. An organism, with phenotype \mathbf{z} , gives rise to a mutant offspring with phenotype $\mathbf{z} + \mathbf{r}$. We assume all n components of \mathbf{r} are generally non-zero, so when a mutation occurs all n characters are generally changed. This model therefore assumes a universal form pleiotropy. In Fisher’s original formulation, a mutation will be adaptive (or beneficial) if the distance of $\mathbf{z} + \mathbf{r}$ from the origin, i.e. $\|\mathbf{z} + \mathbf{r}\|$, is smaller than the parental distance from the origin, $\|\mathbf{z}\|$. The condition for being adaptive can thus be written as $\|\mathbf{z} + \mathbf{r}\|^2 < \|\mathbf{z}\|^2$ and for a given distribution of \mathbf{r} , we can determine the proportion of adaptive mutations from the proportion of all mutations satisfying this condition.

Fisher compared the adaptive nature of mutations with a given magnitude of \mathbf{r} , which we denote by r , i.e., $r = \|\mathbf{r}\|$. He took \mathbf{r} to be uniformly distributed over the surface of a sphere of radius r in n dimensions. As long as the distribution of mutational changes is spherically symmetric (depends only on $\|\mathbf{r}\|$) the proportion of beneficial

mutations, P_{ben} , depends on only a single aspect of the parental phenotype, \mathbf{z} , namely its magnitude (or distance from the optimum), $\|\mathbf{z}\|$. The case of $n = 2$ characters is illustrated in Fig. 1.

Fisher gave an exact result for the proportion of beneficial mutations, P_{ben} , when $n = 3$ and it is possible to write an exact expression for P_{ben} for general n in terms of special functions (see e.g. Kimura, 1983). However for $n \gg 1$ an accurate and convenient approximate expression for P_{ben} was also given by Fisher. It was found to depend only on the combination of parameters

$$\rho_0 = \frac{r\sqrt{n}}{2\|\mathbf{z}\|} \tag{1}$$

and given by

$$P_{\text{ben}}(\rho_0) \simeq \sqrt{\frac{1}{2\pi}} \int_{\rho_0}^{\infty} e^{-u^2/2} du = \frac{1}{2} \text{erfc}\left(\frac{\rho_0}{\sqrt{2}}\right), \tag{2}$$

where $\text{erfc}(\bullet)$ denotes the complementary error function (Abramowitz and Stegun, 1970). The ratio ρ_0 naturally emerges from the calculations and a possibly useful way to view it is as the mutational magnitude, r , divided by a scale that is intrinsic to the problem, which is not $\|\mathbf{z}\|$, but rather $2\|\mathbf{z}\|/\sqrt{n}$.

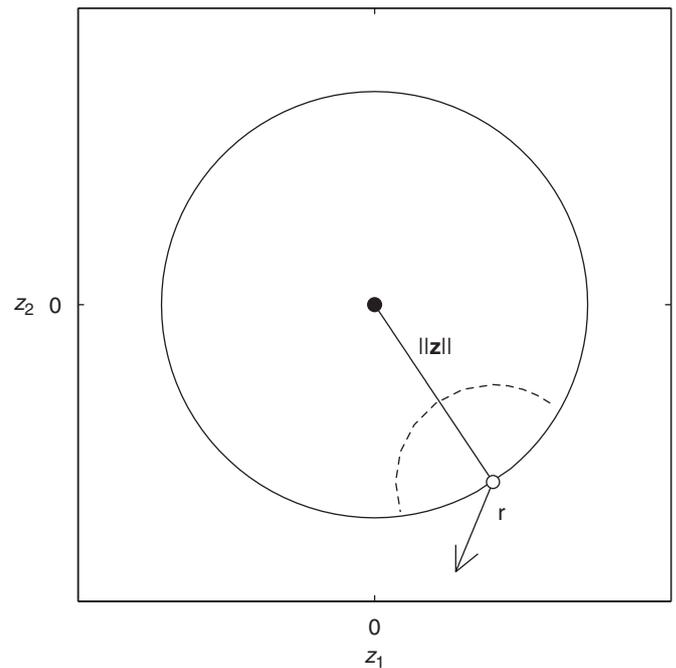


Fig. 1. This figure illustrates Fisher’s geometrical model when there are two traits, z_1 and z_2 , and fitness and mutation are spherically symmetric. The fitness optimum lies at the origin of the coordinate system, $(0, 0)$ and is represented by a filled dot. The unfilled dot represents the phenotype of an individual and the arrow stemming from this point represents a mutational change, of magnitude r . The quantity $\|\mathbf{z}\|$ is the distance of the parental phenotype from the optimum. All points on the solid circle, with radius $\|\mathbf{z}\|$, correspond to the same value of fitness—i.e. they constitute a surface of constant fitness. The dashed arc shows the set of mutations that are closer to the optimum than the parental phenotype and are thus beneficial mutations.

Generalisations of Fisher’s model involve more complicated fitness landscapes (Rice, 1990; Whitlock et al., 2003; Waxman and Welch, 2005; Waxman, 2006; Martin and Lenormand, 2006). In the work of Waxman and Welch (2005), a generalised stabilising-selection fitness function was introduced that was motivated by concerns of Haldane (1932). It takes the form

$$W_G(\mathbf{z}) = \exp\left(-\sum_{j,k=1}^n M_{ij}z_jz_k\right), \quad (3)$$

where M_{ij} are elements of a positive definite symmetric matrix and if, for different i and j , some of the M_{ij} are non-zero, then this form of fitness function represents fitness interactions between different traits. However, compound traits exist that are linear combinations of the existing traits and which simplify the structure of the problem. If we write the compound traits as z_i^* then when these are chosen appropriately, the fitness function of Eq. (3) can be expressed in terms of these compound traits as $\exp(-\sigma_1 z_1^{*2}) \times \exp(-\sigma_2 z_2^{*2}) \times \dots \equiv \exp(-\sum_{j=1}^n \sigma_j z_j^{*2})$, where all $\sigma_j > 0$. Such a fitness function corresponds to selection acting independently, and in a stabilising manner, on the compound traits (Waxman and Welch, 2005). Furthermore, the distribution of mutations, because it has been taken to be spherically symmetric, is completely unaffected by the above “diagonalisation” (which is simply a rotation of the coordinate axes, in the n -dimensional space of traits). In what follows, we shall assume a transformation of the traits appearing in the generalised fitness function, Eq. (3), has been made and that all traits are now compound traits. To reflect the formal similarity of problems with the original traits (as appearing in Eq. (3)) and those expressed in terms of compound traits, we will use the notation \mathbf{z} to refer to *any* collection of traits, regardless of their nature—original or compound. We thus define the fitness $W(\mathbf{z})$ by

$$W(\mathbf{z}) = \exp\left(-\sum_{j=1}^n \sigma_j z_j^2\right). \quad (4)$$

An explicit implication of $W(\mathbf{z})$ is that various properties, e.g., the proportion of beneficial mutations, generally depend on details of \mathbf{z} other than simply its length, $\|\mathbf{z}\|$. The behaviour of the proportion of beneficial mutations is illustrated in Fig. 2, for the case of two traits, and this example explicitly shows a dependence on \mathbf{z} beyond that of $\|\mathbf{z}\|$.

We note that when all σ_j take the same value, say σ , in the fitness function of Eq. (4), then it reduces to $\exp(-\sigma \sum_{j=1}^n z_j^2)$ which can be written $\exp(-\sigma \|\mathbf{z}\|^2)$. This depends only on $\|\mathbf{z}\|$ and is spherically symmetric.

The primary focus of this paper is an accurate treatment of generalised fitness landscapes that are not spherically symmetric. Such landscapes have curvatures which do not take the same value over all points of a surface of constant fitness. In this section, we shall establish sufficient notions of curvature for the analysis presented in this work. More

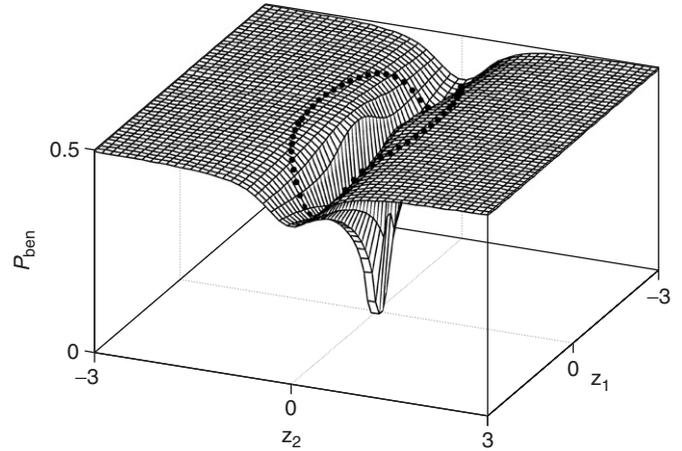


Fig. 2. The figure applies to the case of $n = 2$ traits. The proportion of beneficial mutations, P_{ben} , for the fitness function $W(\mathbf{z}) = \exp(-\sum_{j=1}^2 \sigma_j z_j^2)$ is plotted as a function of the trait values z_1 and z_2 . The strengths of selection on the different traits are $\sigma_1 = 0.15$ and $\sigma_2 = 0.85$. The dashed line is a “surface of constant fitness”—the set of trait values corresponding to the fixed value of fitness $W(\mathbf{z}) = \frac{1}{2}$. Because fitness is not spherically symmetric, the surface of constant fitness is not spherically symmetric, but an ellipse, whose curvature varies from point to point. Furthermore, the proportion of beneficial mutations, P_{ben} , varies over the surface of constant fitness. To produce the figure, mutations were taken to have a spherically symmetric distribution, with a fixed magnitude of $r = 0.4$.

general treatments of curvature can be found in textbooks (see e.g. Kreyszig, 1991).

The curvature, κ , of a circle of radius r is defined as $\kappa = 1/r$. For a more general curve in the x – y plane, which we write as $y = y(x)$, we can determine the curvature at any point by fitting a circle to the point in question. Thus, at any point of interest, we write the formula of the circle we shall fit as $(x - a)^2 + (y - b)^2 = r^2$. This has three unknowns, a , b and r , which have to be found before the circle is determined. We shall use three nearby points on the curve to determine the three unknowns. Taking the x value of the point of interest as x_0 , the three points we shall use are $(x_0 - \varepsilon, y(x_0 - \varepsilon))$, $(x_0, y(x_0))$ and $(x_0 + \varepsilon, y(x_0 + \varepsilon))$. Since the circle passes through these points, we have three equations in three unknowns: $(x_0 - a)^2 + (y(x_0 - \varepsilon) - b)^2 = r^2$ and $(x_0 \pm \varepsilon - a)^2 + (y(x_0 \pm \varepsilon) - b)^2 = r^2$. We then solve these three equations for a , b and r . In the limit $\varepsilon \rightarrow 0$ we obtain the unique circle that makes contact with the curve. With a prime denoting differentiation of a function with respect to its argument, e.g. $y'(x) \equiv dy(x)/dx$, we find that centre of the circle has coordinates (a, b) where $a = (x_0 y''(x_0) - y'(x_0) - [y'(x_0)]^3)/y''(x_0)$, $b = (1 + y''(x_0)y(x_0) + [y'(x_0)]^2)/y''(x_0)$ and the curvature of the curve, at $x = x_0$, is

$$\kappa = 1/r = |y''(x_0)|/(1 + [y'(x_0)]^2)^{3/2} \quad (5)$$

(we do not assign a sign, here, to curvature, and so always take κ as a positive quantity). The formula in Eq. (5) appears to originate with Newton (Rouse Ball, 1960).

As a simple example of this, consider the ellipse $x^2/\alpha^2 + y^2/\beta^2 = 1$. This can be solved for y to yield $y(x)$

which has one of the two sign choices

$$y(x) = \pm \beta \sqrt{1 - x^2/\alpha^2} \quad (6)$$

and a direct application of Eq. (5) leads to a curvature at $x = 0$ of $\kappa = \beta/\alpha^2$.

3. Curvature associated with fitness

Now let us consider the case of a surface of constant fitness, when the fitness function is not spherically symmetric and given by Eq. (4). This form of fitness function was motivated above, in Section 2.

For the purposes of the present work, the most relevant quantity is not $W(\mathbf{z})$ but its natural logarithm, $\log W(\mathbf{z})$, and a surface of constant fitness is also a surface of constant $\log W(\mathbf{z})$ and given by $-\sum_{j=1}^n \sigma_j z_j^2 = -c^2$ where c is a constant. We shall restrict analysis to a particular point of extreme symmetry on such a surface, where elementary considerations of curvature suffice. We shall thus focus interest on the (generally different) $n - 1$ curvatures at a point which has $z_1 \neq 0$ and all other z_j 's vanishing, i.e. the point $(z_1, 0, 0, \dots, 0)$.

At a general point on the surface of constant fitness, z_1 takes one of the two sign choices of

$$z_1 = \pm \frac{1}{\sqrt{\sigma_1}} \sqrt{c^2 - \sum_{j=2}^n \sigma_j z_j^2}. \quad (7)$$

Thus, for example if $z_3 = z_4 = \dots = z_n = 0$ then z_1 is a function only of z_2 which we write as $z_1(z_2)$ and

$$z_1(z_2) = \pm \frac{1}{\sqrt{\sigma_1}} \sqrt{c^2 - \sigma_2 z_2^2}. \quad (8)$$

This is directly analogous to Eq. (6), with $z_1 \rightarrow y$ and $z_2 \rightarrow x$, and the curvature at the point of interest ($z_1 \neq 0$, $z_2 = 0$) is $\kappa_2 = \sigma_2/(\sqrt{\sigma_1}|c|)$. We can simplify this expression by noting that in the limit where all z_j (except z_1) vanish, we have $|c| = \sqrt{\sigma_1}|z_1|$ hence $\kappa_2 = \sigma_2/(\sigma_1|z_1|)$. This quantity represents the curvature, at $z_2 = 0$, of a curve in the z_1 - z_2 plane that is constrained to lie in the surface of constant fitness. More generally, there are $n - 1$ orthogonal directions that pass through the point of interest, $(z_1, 0, 0, \dots, 0)$ in the surface of constant fitness. These correspond to curves that have only z_1 and z_j varying, with j taking only one of $2, 3, \dots, n$, and the explicit value of the local curvature of such a curve, at the point of interest (i.e. where $z_j = 0$) is

$$\kappa_j = \frac{\sigma_j}{\sigma_1|z_1|}, \quad j = 2, 3, \dots, n. \quad (9)$$

See Fig. 3 for an illustration of the case of $n = 3$ characters, and the two different curves through the point $(z_1, 0, 0)$.

The $n - 1$ values of curvature given in Eq. (9) correspond to the principal values of curvature at the point $z_3 = z_4 = \dots = z_n = 0$. At a general point on a surface of

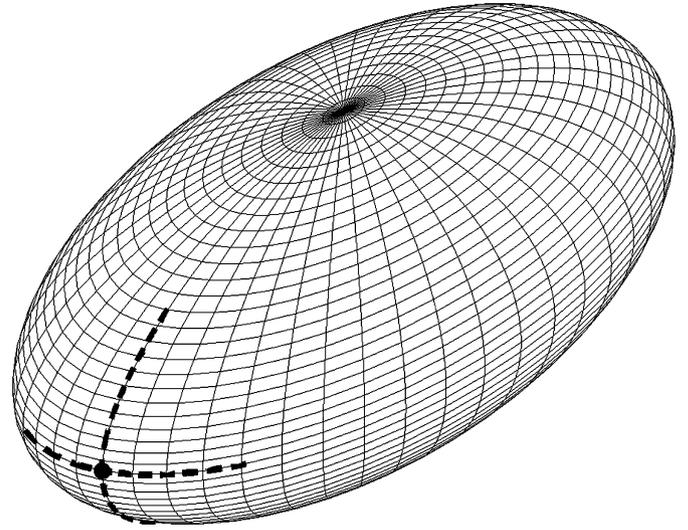


Fig. 3. A surface of constant fitness is illustrated for the case of $n = 3$ traits. The black dot represents the point $(z_1, 0, 0)$ and the two broken curves through this point signify lines in the surface of constant fitness that are in the z_1 - z_2 and z_1 - z_3 planes. The two curvatures, κ_2 and κ_3 (see Eq. (9)) are obtained by fitting circles at $(z_1, 0, 0)$ in these two planes.

constant fitness, the curvatures have a much more complicated expression.

4. Application to generalised versions of Fisher's geometrical model

We now apply the above results to generalised versions of Fisher's geometrical model, where fitness functions are not spherically symmetric. Consider the proportion of mutations, of size r , that are beneficial in a fitness landscape given by Eq. (4). The two approximations we discuss both yield a proportion of beneficial mutations of the form

$$P_{\text{ben}} \simeq \frac{1}{\sqrt{2\pi}} \int_{\rho}^{\infty} e^{-t^2/2} dt = \frac{1}{2} \text{erfc} \left(\frac{\rho}{\sqrt{2}} \right). \quad (10)$$

Here ρ is a dimensionless quantity that characterises mutational changes relative to selection. In the two approximations under consideration, ρ takes different forms. Both of these are generally different to the quantity ρ_0 of Eq. (1).

We note that Rice (1990) was not approximating an identical fitness surface to that associated with Eq. (4)—which is an ellipsoid; Rice's geometry was apparently that of a torus (Rice, 1990). However, it seems reasonable to assume the two approximations should coincide for local quantities—such as the proportion of beneficial mutations, when mutations only probe a small region of a fitness surface.

Proceeding, we interpret Rice's calculation (Rice, 1990) as referring to the curvature of the natural logarithm of fitness, rather than to fitness itself. The resultant

approximation for ρ is ρ_R where

$$\rho_R = \frac{\sqrt{nr}K}{2}, \quad (11)$$

$$K = \left(\frac{1}{n-1} \sum_{\text{curvatures}} \frac{1}{\kappa_j(\mathbf{z})} \right)^{-1} \quad (12)$$

(we assume Rice's Eq. (9) contains a misprint and the factor $n-1$ should lie within the bracket in this equation). The form of Eq. (12) is a particular average curvature: the harmonic mean of the $n-1$ principal curvatures at the point of interest.

In the special case where $z_1 \neq 0$ and all other z_j 's are zero, we use Eq. (9) to reduce ρ_R to:

$$\begin{aligned} \rho_R &= \frac{\sqrt{nr}}{2} \left(\frac{1}{n-1} \sum_{j=2}^n \frac{\sigma_1 |z_1|}{\sigma_j} \right)^{-1} \\ &= \frac{\sqrt{nr}H}{2|z_1|\sigma_1} \quad \text{special case} \end{aligned} \quad (13)$$

where

$$H = \left(\frac{1}{n-1} \sum_{j=2}^n \frac{1}{\sigma_j} \right)^{-1} \quad (14)$$

is the harmonic mean of $\sigma_2, \sigma_3, \dots, \sigma_n$.

By contrast, Waxman and Welch (2005) obtained an alternative approximation from analysis of quantities associated with new mutations in Fisher's geometrical model. This was based on the approximate behaviour of $\log(W(\mathbf{z} + \mathbf{r})/W(\mathbf{z}))$ as a Gaussian random variable (recall that \mathbf{r} is a random mutational change). These authors derived the approximation $\rho \simeq \rho_{WW}$ where

$$\begin{aligned} \rho_{WW} &= \frac{r^2 \bar{\sigma}}{\sqrt{4r^2 \sigma^2 \mathbf{z}^2}} = \frac{r \bar{\sigma}}{2\sqrt{n^{-1} \sum_{j=1}^n \sigma_j^2 z_j^2}} \\ &= \frac{\sqrt{nr} \bar{\sigma}}{2\sqrt{\sum_{j=1}^n \sigma_j^2 z_j^2}}, \end{aligned} \quad (15)$$

where $\bar{\sigma} = \sum_{j=1}^n \sigma_j / n$ is the mean value of the σ_i . Specialising to the case above, namely $z_1 \neq 0$ and all other z_j 's vanishing, we find

$$\rho_{WW} = \frac{\sqrt{nr} \bar{\sigma}}{2|z_1|\sigma_1}, \quad \text{special case.} \quad (16)$$

Note that both ρ_R and ρ_{WW} are of the form $(\sqrt{nr}/2|z_1|)(A/\sigma_1)$ where A is either H (the harmonic mean of $\sigma_2, \sigma_3, \dots, \sigma_n$) or $\bar{\sigma}$ (the arithmetic mean of $\sigma_1, \sigma_2, \dots, \sigma_n$). Note also that when all σ_j are identical, ρ_R and ρ_{WW} (Eqs. (16) and (13)) coincide with one another.

It is evident that generally, ρ_R and ρ_{WW} do not coincide in value. We note that although the arithmetic mean is larger or equal to the harmonic mean, we cannot apply this result here, without further assumptions, and infer that

$\rho_{WW} \geq \rho_R$, since $\bar{\sigma}$ and H refer to different sets of σ 's ($\bar{\sigma}$ involves σ_1 while H does not involve σ_1). However if we view the σ_i as having been drawn from a given probability distribution, then for large n we have, by the law of large numbers, $\bar{\sigma} \rightarrow E[\sigma]$ and $H \rightarrow 1/E[\sigma^{-1}]$, where the expectations, $E[\dots]$, are taken with respect to the probability distribution of the σ 's. The ratio of ρ_{WW} to ρ_R is then given by $\rho_{WW}/\rho_R = E[\sigma]E[\sigma^{-1}]$ and when this result is applicable, the fact that $E[\sigma]E[\sigma^{-1}] \geq 1$ yields $\rho_{WW} \geq \rho_R$.

4.1. Example

As an example, assume the σ 's are drawn from a uniform distribution that ranges from $\sigma_{\min}(>0)$ to σ_{\max} . The coefficient of variation (i.e. standard deviation/mean) of this distribution is given by $\text{CV}(\sigma) = (\sigma_{\max} - \sigma_{\min})/[\sqrt{3}(\sigma_{\max} + \sigma_{\min})]$ and this lies in the range 0 to $1/\sqrt{3} \simeq 0.58$. We find

$$\rho_{WW}/\rho_R = \frac{1}{\sqrt{12}\text{CV}(\sigma)} \ln \left(\frac{1 + \sqrt{3}\text{CV}(\sigma)}{1 - \sqrt{3}\text{CV}(\sigma)} \right) \quad (17)$$

and this is an increasing function of $\text{CV}(\sigma)$.

If the σ 's deviate very little from their mean value, by having a small coefficient of variation, $\text{CV}(\sigma)$, then expanding ρ_{WW}/ρ_R in Eq. (17) to leading non-zero order in $\text{CV}(\sigma)$ yields the approximation $\rho_{WW}/\rho_R \simeq 1 + \text{CV}^2(\sigma)$. For illustrative purposes, let $\sigma_{\min} = 0.7$ and $\sigma_{\max} = 1.3$. This leads to $\text{CV}(\sigma) \simeq 0.17$ and $\rho_{WW}/\rho_R \simeq 1.03$.

Alternatively, suppose there is appreciable variation in the σ 's, by $\text{CV}(\sigma)$ being close to the maximum possible value it can take for a uniform distribution: $\text{CV}(\sigma) \simeq 1/\sqrt{3}$. We then have $\rho_{WW}/\rho_R \simeq \frac{1}{2} \ln(2/(1 - \sqrt{3}\text{CV}(\sigma)))$. To illustrate this, let $\sigma_{\min} = 0.002$ and $\sigma_{\max} = 1.998$, then $\text{CV}(\sigma) \simeq 0.58$ and $\rho_{WW}/\rho_R \simeq 3.46$ i.e., ρ_{WW} is more than three times the size of ρ_R .

5. Numerical test

For the special case where $\mathbf{z} = (z_1, 0, 0, \dots, 0)$, we have numerically tested the two approximations for the proportion of beneficial mutations that result from using either ρ_R (Eq. (13)) or ρ_{WW} (Eq. (16)) in Eq. (10), for P_{ben} .

To set up a numerical test we first invert Eq. (10), to obtain $\rho \simeq \sqrt{2} \text{erfc}^{-1}(2P_{\text{ben}})$, where $\text{erfc}^{-1}(\bullet)$ is the inverse function to $\text{erfc}(\bullet)$. We note that when all σ_i are identical, $\rho \simeq \rho_0$ (ρ_0 is given in Eq. (1)) hence in this case $\rho/\rho_0 \simeq 1$. It is natural, in a more general case, to define a measure of deviations of ρ/ρ_0 from unity, since both approximations generally lead to $\rho/\rho_0 \neq 1$. Accordingly, we define a new quantity R , given by

$$R = \frac{2|z_1|}{\sqrt{nr}} \sqrt{2} \text{erfc}^{-1}(2P_{\text{ben}}). \quad (18)$$

Using the approximation of P_{ben} in Eq. (10) yields $R \simeq 2|z_1|\rho/(\sqrt{nr}) \equiv \rho/\rho_0$, whatever the value of ρ , hence R does indeed measure of deviations of ρ from ρ_0 . The

Table 1
Results of simulations

Row	n	r	σ_{\min}	σ_{\max}	$CV(\sigma)$	H/σ_1	$\bar{\sigma}/\sigma_1$	R
1	50	0.05	1.000	1.000	0.00	1.00	1.00	0.98
2	50	0.05	0.200	1.800	0.46	1.26	1.79	1.78
3	50	0.05	0.002	1.998	0.58	0.41	1.39	1.36
4	50	0.10	1.000	1.000	0.00	1.00	1.00	0.99
5	50	0.10	0.200	1.800	0.46	1.26	1.79	1.78
6	50	0.10	0.002	1.998	0.58	0.41	1.39	1.37
7	100	0.05	1.000	1.000	0.00	1.00	1.00	0.99
8	100	0.05	0.200	1.800	0.46	2.13	3.04	3.02
9	100	0.05	0.002	1.998	0.58	0.27	1.16	1.16
10	100	0.10	1.000	1.000	0.00	1.00	1.00	0.99
11	100	0.10	0.200	1.800	0.46	2.13	3.04	3.00
12	100	0.10	0.002	1.998	0.58	0.27	1.16	1.16

Results of simulations, as described in the main text are given in the Table. Rows 1, 4, 7 and 10, which have $\sigma_{\min} = \sigma_{\max}$, correspond to no variation amongst the σ_i , and serve to show that the R statistic, introduced in Eq. (18), is very close to unity in this case—as predicted by the analytical approximations. In all other rows, R is significantly larger than the approximation following from the work of Rice (H/σ_1), while it is always close to the corresponding result of Waxman and Welch ($\bar{\sigma}/\sigma_1$).

There are significant differences between R values arising from identical distributions of the σ 's, but having different values of n , e.g. the R values given in rows 2 and 8 of the table. Given that in both approximations for ρ , we have that $R \propto 1/\sigma_1$, the differences arise because σ_1 may vary greatly from one set of σ 's to the other, because for different n , the R 's were calculated from independently generated sets of σ 's.

Note that because of the specialisation to $z_1 \neq 0$ in this work, σ_1 has a privileged place in various formulae derived here. However, σ_1 was not distinguished in any way from any other of the σ_i , during the generation of sets of the σ 's. Thus generally, σ_1 is neither the smallest nor the largest of the σ_i but merely a random member of each set of σ 's.

approximation of Rice (1990) yields $R \simeq H/\sigma_1$, while that of Waxman and Welch (2005) yields $R \simeq \bar{\sigma}/\sigma_1$.

To use R as the basis of a numerical test of the value of ρ/ρ_0 , we specialised to the case $z_1 = 1$ and estimated P_{ben} from simulation.

A test of the value of ρ/ρ_0 is carried out with: (i) a given number of traits, n ; (ii) a given magnitude of mutational changes, r ; and (iii) a given set of σ 's, i.e. ($\sigma_1, \sigma_2, \dots, \sigma_n$).

A test of the value of ρ/ρ_0 involves generating a large number of random mutation vectors, \mathbf{r} , with a fixed magnitude of r , and which are uniformly distributed over a sphere in n dimensions. We generated 10^5 random mutation vectors. The proportion of these mutational changes that are beneficial, i.e. the proportion of all \mathbf{r} for which $W(\mathbf{z} + \mathbf{r}) > W(\mathbf{z})$, are determined as an estimate of P_{ben} , which is then used in Eq. (18).

In Table 1 we summarise results of simulations for two different values of the number of traits, n , two different magnitudes of the mutational changes, r , and three different sets of σ 's. For a given n , a particular set of the σ 's was obtained by independently drawing each σ_i from a uniform distribution ranging from σ_{\min} to σ_{\max} . Each set of σ 's was held fixed, for all of the mutational changes used to determine P_{ben} , for the two different values of r .

6. Summary

In this work, we have compared two different approximations of Fisher's geometrical model of evolutionary adaptation. We considered fitness landscapes with surfaces of constant fitness that are not spherically symmetric and hence have different curvatures at different points. The two approximations are rather different in character, and arise from different viewpoints; one manifestly geometrical in nature, the other analytical. The approximation of Rice (1990) is based on a geometric analysis. Because of the qualitative reasoning on which the approximation is based, it is not straightforward to determine its region of validity or its limitations. The approximation of Waxman and Welch (2005) was based on the distribution of the quantity $\log[W(\mathbf{z} + \mathbf{r})/W(\mathbf{z})]$ for fixed \mathbf{z} but random \mathbf{r} . Eq. (4) allows this quantity to be written as $-\sum_{j=1}^n \sigma_j(2z_j r_j + r_j^2)$. The region where a central limit (i.e. Gaussian) sort of behaviour of this sum manifests itself, despite incomplete independence of the different terms, is susceptible to direct analysis (Waxman and Welch, 2005).

We compared the two approximations by focussing on specific points of particular symmetry on a surface of constant fitness. This allowed us to analytically and numerically distinguish the predictions of the two approximations. The two approximations were used to compare the value of the quantity ρ that appears in Eq. (10) and which characterises mutational changes relative to selection. The value of ρ was determined from the proportion of beneficial mutations. Thus, its value was determined from what is a rather subtle feature of the distribution of selection coefficients: the relatively small part of the distribution corresponding to beneficial mutations. As such, a comparison based on ρ provides a stringent test of the approximations. Our findings, for the range of parameters considered in this work, indicate that when there is variation in the strengths of selection on different traits (the σ_i) the Gaussian approximation of Waxman and Welch (2005) (see also Waxman, 2006) is very close to the results of simulations and significantly different to the "average curvature" approximation of Rice (1990).

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