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Mathematical Biosciences 194 (2005) 81–93
Mathematical Biosciences
www.elsevier.com/locate/mbs

Dynamics of a quantitative character subject only to stabilising selection

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Received 3 May 2004; received in revised form 16 November 2004; accepted 16 November 2004

Abstract

The implications of stabilising selection on a quantitative trait, in the absence of other evolutionary forces, are theoretically investigated in a randomly mating population. The dynamics of various statistics that describe the alleles contributing to the trait are determined and used to infer the behaviour of the trait.

Dynamical solutions of the distribution of allelic effects and the distribution of the trait are found when all initial distributions of allelic effects are Gaussian and linkage disequilibria are neglected. Some results for the behaviour of the mean and the variance of genotypic effects of the population, when subject to a moving optimum, are derived.

When the initial distributions of allelic effects are not Gaussian, but possess a small asymmetry, the mean and the variance of the allelic effects differ only slightly from the Gaussian results. By contrast, the third central moments of allelic effects, are, at all loci, strictly zero in the Gaussian case but are generally non-zero for non-symmetric initial distributions. To leading order in a quantitative measure of the asymmetry of the distribution, we determine the third central moment of allelic effects.

Keywords: Stabilising selection; Population dynamics; Quantitative trait; Non-Gaussian behaviour

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doi:10.1016/j.mbs.2004.11.009

1. Introduction

Many of the traits that are significant for subjects such as evolutionary adaptation, have a polygenic origin and constitute continuously varying quantitative characters. In this work we consider a population, where, during the time-scales of interest, only stabilising selection on a quantitative trait is of importance and other evolutionary processes such as mutation, genetic drift, and migration can be neglected. In this case, the selection-driven dynamics of pre-existing genetic variation is the primary focus of attention and we investigate some of the possible transient phenomena that such a population can experience.

Fully understanding such a model should also prove useful in understanding more complex models, where purely selective phenomena inevitably become entangled with other processes such as mutation. This, ultimately, is the motivation for this work, since there are aspects of dynamics involving selection on a quantitative trait that remain obscure and require further clarification and understanding. As an example, results involving biased mutation [1] indicate that selection at the trait level can be effectively *evaded*, at the gene level. This means that while the trait equilibrates, there may be an allelic turnover (or running of allelic effects) that continuously occurs in a large population – at least until genetic variation is exhausted or some sort of genetic constraint manifests itself [1].

The present investigation is made in the framework of a sexual, diploid model with a continuum of alleles, where a quantitative trait is additively determined from allelic effects of a number of unlinked loci [2,3]. If a Gaussian or similar function of genotypic values is adopted to describe fitness then there are only a small number of parameters characterising the model, namely a measure of the intensity of selection, the number of loci and the optimal phenotypic value. These parameters are not, however, the whole story. The initial distribution of the population generally has a substantial influence on the population's subsequent dynamics, since no new variation originates during the time-interval of interest and all that can occur is an irreversible change of the population over time.

The model described above appears to be one of the simplest descriptions of a quantitative character, with only selection of a particularly simple type occurring. Indeed, one might expect to find such a model solved in text-books on quantitative genetics, but this is not the case, perhaps because despite the conceptual simplicity of the problem, it is not mathematically trivial. In particular the dynamical equations are intrinsically non-linear and possess a degree of mathematical complexity since selection at any locus is influenced by the genetic background of that locus.

Apart from the classic paper of Robertson [4], on the effects of stabilising selection on genetic variation, other more recent studies of explicitly dynamical phenomena have considered aspects of strong selection [5,6], the complex response of populations to change of the optimal phenotype [7] and the dynamics at the phenotypic level [8].

2. Model

Consider an effectively infinite population of sexual organisms that are diploid, randomly mating and dioecious. Individuals do not exhibit any sexual dimorphism, and are characterised by a single phenotypic trait that is controlled by $2n$ alleles at n unlinked loci. We assume additive genet-

ics, where an individual's genotypic value is given by $G = \sum_{j=1}^{n}(x_j + y_j)$, where x_j (y_j) is the effect of the maternally (paternally) originating allele at locus j. Thus at the level of the trait, there is no dominance or epistasis. Following Crow and Kimura [2], Kimura [3] and many subsequent authors, we take allelic effects, such as x_j, to be continuous and range from $-\infty$ to ∞. Allelic effects are also used as a unique label of different alleles.

Fitness is taken to be determined entirely by stabilising viability selection on the phenotypic value of the trait. Phenotypes consists of a sum of a genotypic value and a statistically independent random environmental effect that is normally distributed, with mean zero and variance unity. The viability of individuals of genotypic value G arises from an average over environmental effects (see e.g. [9]). If a noroptimal selection scheme [10] is adopted, then relative to the fittest individuals, the viability has the form $\exp[-s(G - G_{\mathrm{opt}})^2]$, where s is a positive constant characterising the intensity of selection and G_{opt} is the optimal genotypic value (which coincides with the optimal phenotypic value). Generally, G_{opt} depends on time t, although we shall only show this time dependence when it clarifies matters.

When only small values of $(G - G_{\mathrm{opt}})^2$ occur with any appreciable frequency, as we shall assume, the noroptimal viability may be well approximated by

$$w(G) = 1 - s(G - G_{\mathrm{opt}})^2 \tag{1}$$

and this is the form of relative fitness that we shall adopt in what follows.

We assume discrete generations, weak selection ($s \ll 1$, $s\,\mathrm{Var}(G) \ll 1$, where $\mathrm{Var}(G)$ is the variance of G) as is appropriate to naturally occurring populations [11] and neglect linkage disequilibria. Investigations of the full multilocus problem indicate that neglect of linkage disequilibria is a very reasonable approximation when selection is weak (see e.g. [9,12]).

Census is made at the zygotic stage, prior to the action of selection. At the time of census, the population is in Hardy–Weinberg equilibrium. The consequence of this, and the neglect of linkage disequilibria, is the statistical independence of all alleles both across and between loci.

Let $\phi_j(x,t)$ denote the probability density of allelic effects of maternal origin at locus j in generation t. Apart, possibly, from the first generation, the distributions of allelic effects of paternal and maternal origin coincide, as we shall henceforth assume. Given that the intensity of selection, s, is small, it follows that the difference between $\phi_j(x,t)$ and $\phi_j(x,t+1)$ is also small and a continuous-time approximation is justified. We can then replace $\phi_j(x,t+1) - \phi_j(x,t)$ by $\partial\phi_j(x,t)/\partial t$ and from this and the description of the model, we arrive at a dynamical equation for $\phi_j(x,t)$. The resultant equation coincides with the continuous time equation, associated with a Malthusian fitness function that depends quadratically on trait values, and reads

$$-\partial\phi_j(x,t)/\partial t = s\left[(x - \bar{x}_j + \overline{G} - G_{\mathrm{opt}})^2 - \overline{(x_j - \bar{x}_j + \overline{G} - G_{\mathrm{opt}})^2}\right]\phi_j(x,t). \tag{2}$$

Here overbars denote an average appropriate to generation t, e.g. $\bar{x}_j = \int x\phi_j(x,t)\,\mathrm{d}x$, $\overline{G} = 2\sum_{j=1}^{n}\bar{x}_j$ and $\overline{(x_j - \bar{x}_j + \overline{G} - G_{\mathrm{opt}})^2} = \int (x - \bar{x}_j + \overline{G} - G_{\mathrm{opt}})^2\phi_j(x,t)\,\mathrm{d}x$ (we use the convention, both here and elsewhere, that all integration variables range from $-\infty$ to ∞, unless explicitly stated to the contrary).

3. Basic properties of the long time dynamics

Basic properties of Eq. (2) may be inferred, when $G_{\rm opt}$ is independent of time and we make the assumption (borne out by numerical approaches) that the solution equilibrates at long times. In such a case, as $t \to \infty$, quantities approach equilibrium values: $\bar{x}_j(t) \to \hat{\bar{x}}_j$, $\overline{G}(t) \to \widehat{\overline{G}}$ and $\phi_j(x,t) \to \hat{\phi}_j(x)$. Then Eq. (2) collapses to $(x - \hat{\bar{x}}_j + \widehat{\overline{G}} - G_{\rm opt})^2 \hat{\phi}_j(x) = \overline{(x - \hat{\bar{x}}_j + \widehat{\overline{G}} - G_{\rm opt})^2 \hat{\phi}_j(x)}$ and the only way this equation can hold and also be consistent with $\int x \hat{\phi}_j(x)\,{\rm d}x = \hat{\bar{x}}_j$ is if (i) $\hat{\phi}_j(x) = \delta(x - \hat{\bar{x}}_j)$ where $\delta(\bullet)$ denotes a Dirac delta function and (ii) $\widehat{\overline{G}} = G_{\rm opt}$. This means that for a static $G_{\rm opt}$, the assumption of equilibrium ultimately results in a monomorphic population where the mean trait value coincides with the optimal phenotypic value and at any given locus, all individuals have the same allele.

While the assumption of equilibrium determines the value of the sum of mean allelic effects: $2\sum_j \hat{\bar{x}}_j = G_{\rm opt}$, it does not determine unique values of the mean allelic effects, $\hat{\bar{x}}_j$, at different loci: the values of the $\hat{\bar{x}}_j$ depend on parameters in the initial distribution $\phi_j(x,0)$, as is shown below.

4. Formal solution of the dynamical equation

The solution of Eq. (2) is shown in Appendix A to be

$$\phi_j(x,t) = \frac{\exp[-st(x - F_j(t))^2]\phi_j(x,0)}{\int \exp[-st(y - F_j(t))^2]\phi_j(y,0){\rm d}y}, \tag{3}$$

where $F_j(t) = t^{-1}\int_0^t [\bar{x}_j(v) - (\overline{G}(v) - G_{\rm opt}(v))]\,{\rm d}v$.

We view Eq. (3) as only a formal solution of the problem, since $\phi_j(x,t)$ is given in terms of the function $F_j(t)$. However $F_j(t)$ depends on time averages of $\bar{x}_j$ and $\overline{G}$ and these require knowledge of the unknown distribution $\phi_j(x,t')$ for values of t' earlier than t. Working analytically, we have found that the formal solution, Eq. (3), is a useful way of proceeding. In doing so, we note that a feature of Eq. (3) is that the distribution at time t is significantly influenced by the initial distribution and in what follows, we make the assumption that for all loci, $\phi_j(x,0)$ is continuous and non-vanishing over $\infty > x > -\infty$ (a property possessed, for example, by a Gaussian distribution). Forms of $\phi_j(x,0)$ that consist of just a sum of Dirac delta functions lead to results equivalent to a model with only discrete alleles and are not covered in the present work.

5. Initial distribution

An exactly soluble case of Eq. (3) follows, when all initial distributions, $\phi_j(x,0)$, are taken to be Gaussian distributions. In this case all $\phi_j(x,t)$ (for all $t > 0$) are Gaussian distributions and below, we give the variance of these distributions and the equations that determine their means. However, an initial distribution that is completely symmetric about its mean, of which a Gaussian is an example, is a rather special and possibly contrived situation. Thus to increase the generality of the analysis presented, we consider the properties of the population, when the initial distributions of allelic effects posses a non-zero level of asymmetry. We shall adopt initial distributions

that deviate from a Gaussian – yet are sufficiently 'close' to a Gaussian, that we can exploit the exact solubility arising when all distributions are initially Gaussian.

We take the initial distribution to be

$$\phi_{j,\varepsilon}(x,0) = \frac{2}{\sqrt{1+\varepsilon_j}+\sqrt{1-\varepsilon_j}}\sqrt{\frac{1}{2\pi\sigma_j^2}} \times \begin{cases} \exp\left(-\dfrac{(x-a_j)^2}{2\sigma_j^2(1+\varepsilon_j)}\right), & x > a_j, \\ \exp\left(-\dfrac{(x-a_j)^2}{2\sigma_j^2(1-\varepsilon_j)}\right), & x < a_j. \end{cases} \tag{4}$$

This is continuous for all values of x, but for $\varepsilon_j \neq 0$ is asymmetric. An example of this distribution is plotted in Fig. 1.

Initial distributions of the type in Eq. (4) lead to very complex expressions, hence to simplify matters, we shall assume all 'asymmetry parameters,' ε_j, are small in magnitude: $|\varepsilon_j| \ll 1$. For all quantities of interest, we shall calculate only the leading non-zero term, in an expansion in the ε_j. For our purposes, this entails keeping terms no higher than linear order in the ε_j. Neglecting terms of $O(\varepsilon_j^2)$ and higher order is equivalent to working with an initial distribution that follows from Eq. (4) by expansion in ε_j, namely

$$\phi_{j,\varepsilon}(x,0) = \phi_{j,0}(x,0) \times \begin{cases} 1+\dfrac{\varepsilon_j}{2\sigma_j^2}(x-a_j)^2, & x > a_j, \\ 1-\dfrac{\varepsilon_j}{2\sigma_j^2}(x-a_j)^2, & x < a_j, \end{cases} \tag{5}$$

where $\phi_{j,0}(x,0) = (2\pi\sigma_j^2)^{-1/2}\exp(-(x-a_j)^2/(2\sigma_j^2))$.

While the distribution of Eq. (5) is not positive everywhere, it contains the leading two terms, in an expansion in ε_j, of a genuinely positive distribution. Consequently, its usage correctly gives the expected value of quantities, to linear terms in ε_j.

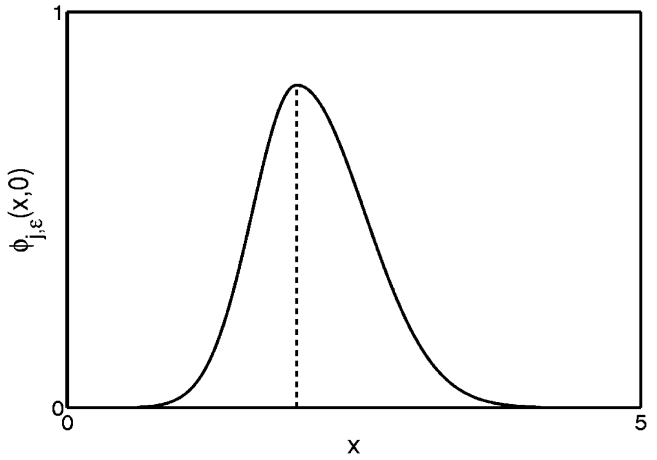

Fig. 1. The initial distribution of allelic effects, $\phi_{j,\varepsilon}(x,0)$, of Eq. (4), is plotted against allelic effect, x. The plot illustrates a case where $\varepsilon_j \neq 0$ so the distribution is not symmetric about its maximum, which occurs at $x = a_j$. The parameter values adopted are $\varepsilon_j = 0.4$, $\sigma_j = 0.5$ and $a_j = 2$.

6. Results for various statistics

6.1. Definitions

We shall concentrate on three important statistics of allelic effects that describe the population, namely the mean, the variance and the third central moment about the mean. These are defined by $\bar{x}_j \equiv \bar{x}_j(t) = \int x\phi_j(x,t)\,\mathrm{d}x$, $v_j \equiv v_j(t) = \overline{(x-\bar{x}_j)^2} = \int (x-\bar{x}_j)^2\phi_j(x,t)\,\mathrm{d}x$ and $\mu_{3j} \equiv \mu_{3j}(t) = \overline{(x-\bar{x}_j)^3} = \int (x-\bar{x}_j)^3\phi_j(x,t)\,\mathrm{d}x$. From these results we can determine the corresponding statistics describing the trait: $\overline{G} = 2\sum_{j=1}^{n}\bar{x}_j$, $\mathrm{Var}_t(G) = \overline{(G-\overline{G})^2} = 2\sum_{j=1}^{n} v_j$ and $\overline{(G-\overline{G})^3} = 2\sum_{j=1}^{n}\mu_{3j}$; the last two results following from Hardy–Weinberg equilibrium and the neglect of linkage disequilibria.

6.2. Results for time $t = 0$

For aid of comparison, we have determined the corresponding moments of allelic effects at time $t = 0$. Keeping only the leading non-zero term, in an expansion in ε_j, we find, from Eq. (5), that $\bar{x}_j(0) = a_j + \mathrm{O}(\varepsilon_j)$, $v_j(0) = \sigma_j^2 + \mathrm{O}(\varepsilon_j^2)$ and $\mu_{3j}(0) = \sqrt{\frac{2}{\pi}}\sigma_j^3\varepsilon_j + \mathrm{O}(\varepsilon_j^3)$ and in what follows, we assume that a_j and σ_j are not small compared with ε_j (i.e. a_j and σ_j are $\mathrm{O}(\varepsilon_j^0)$ for all j).

6.3. Results for times $t > 0$

For fixed t, the mean allelic effect, $\bar{x}_j(t)$, and the variance in allelic effects, $v_j(t)$ both remain finite as $\varepsilon_j \to 0$ (see Appendix B for details of all calculations for this subsection). Thus, just like their $t = 0$ counterparts, they are both non-zero to $\mathrm{O}(\varepsilon_j^0)$ and are the leading non-zero terms, in an expansion in ε_j. By contrast, the third central moment, $\mu_{3j}(t)$, vanishes as $\varepsilon_j \to 0$, and in an expansion in ε_j, the term linear in ε_j is the leading non-zero term. We write $\bar{x}_j(t) = \bar{x}_{j,0}(t) + \mathrm{O}(\varepsilon_j)$, $\overline{G}_0(t) = 2\sum_{j=1}^{n}\bar{x}_{j,0}(t)$ so $\overline{G}(t) = \overline{G}_0(t) + \mathrm{O}(\varepsilon)$ and $v_j(t) = v_{j,0}(t) + \mathrm{O}(\varepsilon_j)$. Then with

$$\Lambda_j \equiv \Lambda_j(t) = (1 + 2s\sigma_j^2 t)^{-1} \tag{6}$$

the variance in allelic effects, to zeroth order in ε_j, is

$$v_{j,0}(t) = \sigma_j^2\Lambda_j(t). \tag{7}$$

The mean allelic effect, to zeroth order in ε_j, namely $\bar{x}_{j,0}$, follows from solution of

$$\mathrm{d}\bar{x}_{j,0}(t)/\mathrm{d}t = -2sv_{j,0}(t)[\overline{G}_0(t) - G_{\mathrm{opt}}(t)] \tag{8}$$

subject to the initial condition $\bar{x}_{j,0}(0) = a_j$.

The quantities $\bar{x}_{j,0}(t)$ and $v_{j,0}(t)$ are the mean and the variance of allelic effects, to zeroth order in ε_j. They can be directly calculated by taking $\varepsilon_j = 0$ in all initial distributions of allelic effects, i.e. by taking all initial distributions to be Gaussian. They correspond to the mean and the variance of the resulting distributions of allelic effects, which are all Gaussian, for all times.

A quantity that is substantially more complicated than $\bar{x}_{j,0}(t)$ and $v_{j,0}(t)$ is the third central moment of allelic effects, μ_{3j}. To leading non-zero order in the asymmetry parameter ε_j, we find μ_{3j} has the time dependent form

$$\mu_{3j}(t) = \varepsilon_j \sqrt{\frac{2}{\pi}} \sigma_j^3 \Lambda_j^{5/2} \exp\left(-\frac{(a_j - \bar{x}_{j,0})^2}{2\sigma_j^2 \Lambda_j} \right) + \mathrm{O}(\varepsilon_j^2). \tag{9}$$

We discuss a special case of μ_{3j} in the following section.

The procedure used to actually solve Eq. (8) for $\bar{x}_{j,0}(t)$, is to sum twice Eq. (8) over all j. This yields the following equation for the mean trait value, to zeroth order in ε:

$$\mathrm{d}\overline{G}_0(t)/\mathrm{d}t = -4s \left(\sum_{j=1}^{n} \sigma_j^2 \Lambda_j \right) [\overline{G}_0 - G_{\mathrm{opt}}]. \tag{10}$$

This linear equation may be solved for $\overline{G}_0$ and the result, when used in Eq. (8), allows $\bar{x}_{j,0}(t)$ to be determined by direct integration.

The variance of the trait is given by

$$\mathrm{Var}_t(G) = 2 \sum_{j=1}^{n} v_{j,0}(t) + \mathrm{O}(\varepsilon). \tag{11}$$

When all $\varepsilon_j = 0$, the reduction of the variance of the trait, with time, as seen from Eqs. (6) and (11), is in accordance with the result of Schnol and Kondrashov [13], for the effect of selection on genetic variance.

The trait also has a generally non-zero (time dependent) third central moment that is given by

$$\overline{(G - \overline{G})^3} = 2 \sum_{j=1}^{n} \mu_{3j} = 2 \sum_{j=1}^{n} \varepsilon_j \sqrt{\frac{2}{\pi}} \sigma_j^3 \Lambda_j^{5/2} \exp\left(-\frac{(a_j - \bar{x}_{j,0})^2}{2\sigma_j^2 \Lambda_j} \right) + \mathrm{O}(\varepsilon^2). \tag{12}$$

Since the trait is additively determined from allelic effects, it follows, from Hardy–Weinberg equilibrium and the approximation of linkage equilibrium, that to zeroth order in asymmetry, the trait is normally distributed with mean $\overline{G}_0(t)$ and variance $2\sum_{j=1}^{n} v_{j,0}(t)$.

We note that an equation equivalent to Eq. (10) has appeared in the approximate analysis of Barton and Turelli [8] – see their Eq. (5.2). Their accompanying differential equation for the variance, which in our notation reads $\mathrm{d}\,\mathrm{Var}_t(G)/\mathrm{d}t \simeq -s[\mathrm{Var}_t(G)]^2/n$ (derived from their Eqs. (5.2) and (6.3)) only follows from Eq. (11) when all initial allelic variances, i.e. all σ_j^2, are identical at all loci. When this is not the case, and all allelic variances are not initially identical, then allelic variances at different loci change at different rates and generally, no differential equation for $\mathrm{Var}_t(G)$ appears to exist. Also, in contrast to the approach of Barton and Turelli [8], we have not assumed a 'moment closure' scheme, where high moments are expressed in terms of lower moments. Rather we have consistently worked out the moments, to leading non-trivial order, in a controlled expansion in a parameter characterising the asymmetry of the initial distribution.

7. Special case

The results of the previous section lead to somewhat complicated expressions for all quantities other than the variances of allelic or genotypic effects. To simplify matters, we shall therefore

consider a special case where the optimal phenotypic value, $G_{\rm opt}$ is independent of time and where all initial allelic variances, σ_j^2, have the same value, namely σ^2. We then find that Eq. (10) yields

$$\overline{G}_0(t) = G_{\rm opt} + (1 + 2s\sigma^2 t)^{-2n}\big(\overline{G}_0(0) - G_{\rm opt}\big). \tag{13}$$

It follows from this result and Eq. (8) that

$$\bar{x}_{j,0}(t) = a_j - (\overline{G}_0(0) - G_{\rm opt})[1 - (1 + 2s\sigma^2 t)^{-2n}]/(2n). \tag{14}$$

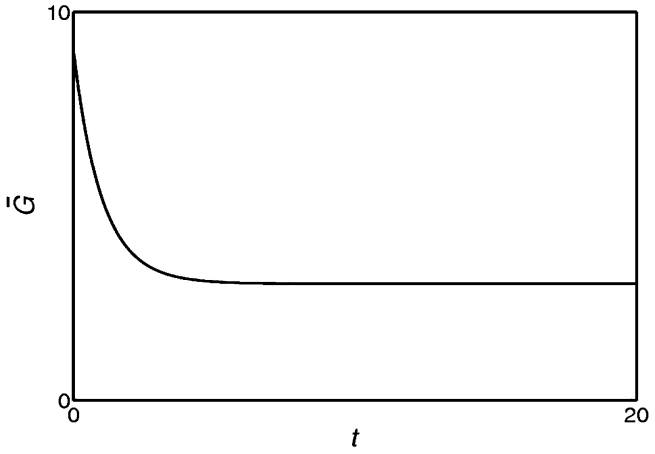

Fig. 2. The mean trait value of Eq. (13) is plotted against time, t, for the case where all initial allelic distributions are Gaussian. For the case illustrated, the distributions of allelic effects of all loci are taken to have identical standard deviations. Parameter values adopted are $\overline{G}_0(0) = 9$, $G_{\rm opt} = 3$, $s = 0.05$, $\sigma = 0.5$ and $n = 20$.

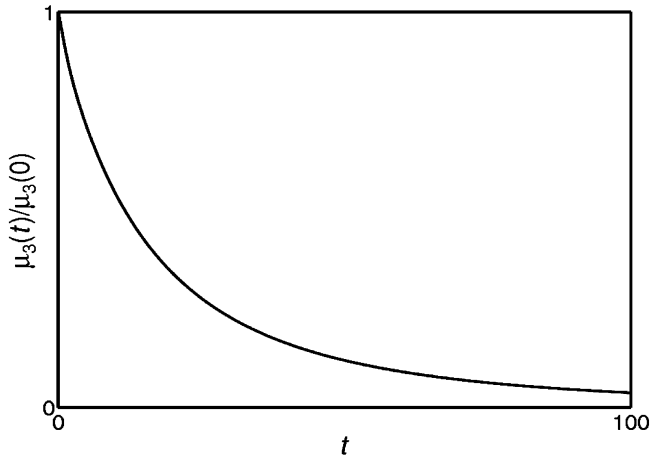

Fig. 3. The third central moment, of the trait, relative to its value at time $t = 0$, $\mu_3(t)/\mu_3(0)$, is plotted against time, t. The case illustrated corresponds to the result of Eq. (15), which was calculated for the case where the distributions of allelic effects of all loci have identical standard deviations. Parameter values adopted are $\overline{G}_0(0) = 9$, $G_{\rm opt} = 3$, $s = 0.05$, $\sigma = 0.5$ and $n = 20$.

We thus have explicit information on the way $\overline{G}_0(t)$ and $\bar{x}_{j,0}(t)$ approach their equilibrium values, namely both approach them as t^{-2n}. Furthermore, at large times, $\bar{x}_{j,0}(t)$ approaches $a_j - (\overline{G}_0(0) - G_{\rm opt})/(2n)$, and is thus determined from the initial state of the population.

Fig. 2 contains an illustration of how $\overline{G}_0(t)$ changes with time.

For the special case of this section, $\sigma_j = \sigma$, $\Lambda_j = \Lambda \equiv (1 + 2s\sigma^2 t)^{-1}$ and all μ_{3j}'s are identical. We can then write $\overline{(G - \overline{G})^3} = 2n\mu_3$ where

$$\mu_3(t) \simeq \varepsilon\sqrt{\frac{2}{\pi}}\sigma^3 \Lambda^{5/2} \exp\left(-\frac{\left(1-\Lambda^{2n}\right)^2}{2\Lambda}\left(\frac{\overline{G}_0(0) - G_{\rm opt}}{2n\sigma}\right)^2\right). \tag{15}$$

We note that irrespective of the value of $\overline{G}_0(0)$, $\mu_3(t)$ vanishes, at large t, at least as fast as $t^{-5/2}$, because of the $\Lambda^{5/2} \equiv (1 + 2s\sigma^2 t)^{-5/2}$ factor in Eq. (15).

In Fig. 3 we have plotted $\mu_3(t)/\mu_3(0) \propto \overline{(G - \overline{G})^3}$ as a function of time.

8. Special case

As a second special case, we shall consider how the population responds to a varying phenotypic optimum when initially, all allelic distributions are Gaussian and have identical variances, i.e. $\varepsilon_j = 0$ and $\sigma_j^2 = \sigma^2$ and $\Lambda_j = \Lambda(t) \equiv (1 + 2s\sigma^2 t)^{-1}$ for all j.

We then find, from Eq. (11) that, independent of the behaviour of $G_{\rm opt}$, the variance is $2n\sigma^2/(1 + 2s\sigma^2 t) = 2n\sigma^2\Lambda(t)$, i.e. it continuously decreases with time, t. The mean genotypic value, for this case, can be written as

$$\begin{aligned}\overline{G}_0(t) &= \Lambda^{2n}(t)\overline{G}_0(0) + 4ns\sigma^2 \int_0^t \frac{\Lambda^{2n}(t)}{\Lambda^{2n-1}(u)} G_{\rm opt}(u)\,{\rm d}u \\ &= G_{\rm opt}(t) + \Lambda^{2n}(t)[\overline{G}_0(0) - G_{\rm opt}(0)] - \Lambda^{2n}(t)\int_0^t \Lambda^{-2n}(u)\frac{{\rm d}G_{\rm opt}(u)}{{\rm d}u}\,{\rm d}u.\end{aligned} \tag{16}$$

This last form indicates that if ${\rm d}G_{\rm opt}(t)/{\rm d}t > 0$ then at large t, when initial information has decayed away, $\overline{G}_0(t) < G_{\rm opt}(t)$. For example, if $G_{\rm opt}(t) = a + bt$ then $\overline{G}_0(t) \simeq (a - b/[2s\sigma^2(2n+1)]) + bt[2n/(2n+1)]$ which is less than $a + bt$ when $b > 0$.

Generally, we infer that in the pure Gaussian case, the variance decreases, independently of what the optimal phenotype does and the mean genotypic value lags behind a linearly increasing optimal phenotypic value. The mean relative fitness, $\bar{w}(t) = 1 - s[\overline{G}_0(t) - G_{\rm opt}(t)]^2 - s\,{\rm Var}_t(G)$ will, asymptotically, be dominated by $1 - s[\overline{G}_0 - G_{\rm opt}]^2$ since the variance term vanishes rapidly at large t. In the case of a linearly increasing optimal phenotype: $G_{\rm opt}(t) = a + bt$, the fitness will decrease quadratically with time since $[\overline{G}_0 - G_{\rm opt}]^2 = [b((2s\sigma^2)^{-1} + t)/(2n+1)]^2$. Of course the approximate form of fitness given in Eq. (1) will not be valid indefinitely, when fitness declines quadratically with time.

9. Discussion

In this work we have performed an analysis where essentially the only approximation was the neglect of linkage disequilibria – an approximation that other studies have validated. We have

shown that in the presence of stabilising selection, but in the absence of mutation etc., the initial state of a large population influences both its dynamics and – in the case of a static phenotypic optimum – its ultimate equilibrium. We have considered initial conditions that corresponds to allelic distributions being close to a Gaussian distribution. When all initial allelic distributions are *exactly* Gaussian, the resulting distributions at later times remain Gaussian. While the mean genotypic value was found to depend on the history of the optimal phenotypic value, $G_{\rm opt}$, the genetic variance was independent of any changes in $G_{\rm opt}$. Given that the genetic variance asymptotically decreases as $1/t$ ($t =$ time), this indicates that in such a Gaussian case, any motion of the optimal phenotypic value cannot maintain genetic variation in the population. If the analysis is extended to include leading corrections arising from a small initial asymmetry of the allelic distributions, then following from Appendix B, we obtain a variance that to linear order in ε_j is given by: $v_j = \Lambda_j\sigma_j^2\left[1 - \varepsilon_j\Lambda_j \mathrm{erf}((a_j - \langle x\rangle_{j,0})/\sqrt{2\sigma_j^2\Lambda_j})\right]$. The quantity $a_j - \langle x\rangle_{j,0}$ can be negative or positive, thus to linear order in ε_j we have the bound $\Lambda_j\sigma_j^2(1+\varepsilon_j\Lambda_j) > v_j > \Lambda_j\sigma_j^2(1-\varepsilon_j\Lambda_j)$. Since at large times, Λ_j vanishes as $1/t$, we find that to linear order in ε_j, and independent of the movement of $G_{\rm opt}$, v_j still asymptotically approaches zero as $1/t$.

When $G_{\rm opt}$ is static, we have found that in the Gaussian case, the mean value of the trait approaches its equilibrium value (of $G_{\rm opt}$) as a power of time: $\overline{G} - G_{\rm opt} \sim t^{-2n}$ where n is the number of loci. Indeed the power law approach of the genotypic value to equilibrium can be directly attributed to the power law behaviour of the genetic variance (see Eqs. (10) and (11)). When $G_{\rm opt}$ has a fixed rate of change, we find that the mean trait value cannot keep up with the moving optimum, unlike what can happen when mutation occurs [14] and as a consequence, genetic loads increase over time – ultimately to unsustainable levels.

This work has also allowed analytic access to the third central moment of allelic effects and the third central moment of genotypic effects. Such terms exist only because the initial distributions of allelic effects are asymmetric, and for the form of asymmetry considered here, the third central moments fell off rapidly with time, t, at least as quickly as $t^{-5/2}$. This indicates that third central moments will not exist for a long time, unless there is an input into them via some of the evolutionary processes we have omitted from consideration. We note that third central moments are crucial for some of the non-monotonic behaviour seen in the theory of biased mutation [1].

Let us conclude, with a brief discussion of the solutions we have found for the equation that determines the behaviour of the distributions of allelic effects, Eq. (2). We restrict discussion to the case where all distributions of allelic effects are initially – and at later times – Gaussian. Since we are in the position of possessing solutions, it is worthwhile to explore some of their properties. Perhaps, the most interesting seems to be what happens when we make the replacement $s \to -s$ in Eq. (2). In this case the fitness function takes the form $w(G) = 1 + s(G - G_{\rm opt})^2$ and corresponds to selection not being stabilising, but rather of a disruptive type. Note that now, $G = G_{\rm opt}$ corresponds to the fitness *minimum* and $w(G)$ has the interpretation as the viability, relative to individuals with the *minimum* viability.

With the replacement $s \to -s$ the Gaussian distributions of allelic effects, found previously, continue to apply. Without addressing questions about the range of parameters where linkage disequilibria remain neglectable (which requires a separate analysis), we note that the solutions obtained cease to be meaningful for times larger than $t_0 = \min_j(2s\sigma_j^2)^{-1}$. This natural boundary

in time arises since the variance of locus j is now proportional to $(1-2s\sigma_j^2 t)^{-1}$ and this ceases to be positive and hence correspond to a meaningful solution for $t > (2s\sigma_j^2)^{-1}$. Thus one or more of the allelic distributions cease to be non-negative for $t > t_0$ and there is a breakdown at $t = t_0$. Indeed, as t approaches t_0 from below, it may be verified that the variance of one (or more) of the allelic distributions diverges and that generally $\overline{G}_0(t)$ diverges. Such divergent behaviour is a genuine feature, and not an artefact of any approximations that lead to Eq. (2); it even occurs in simple, one locus asexual models that evolve in discrete time, as may be simply demonstrated from dynamics of the form $\phi(x,t+1) = w(x)\phi(x,t)/\int w(x)\phi(x,t)\,\mathrm{d}x$, with $w(x) = \exp(sx^2)$ $(s>0)$ and $\phi(x,0) \propto \exp(-x^2/(2\sigma^2))$. The solution, at generation t, is $\phi(x,t) = [w(x)]^t\phi(x,0)/\int[w(x)]^t\phi(x,t)\,\mathrm{d}x$ and this also ceases to be meaningful for times t larger than $(2s\sigma^2)^{-1}$.

Acknowledgment

It is a pleasure to thank John Welch for helpful discussions. This work was supported by the Leverhulme Trust.

Appendix A

In this appendix, we derive Eq. (3), which is the formal solution to the dynamical equation, Eq. (2). It is convenient to introduce $F_j(t) = \frac{1}{t}\int_0^t(\bar{x}_j(u) - [\overline{G}(u) - G(u)])\,\mathrm{d}u$. This allows us to write the right hand side of Eq. (2) as $\partial[sx^2t - 2sxtF_j(t) - \psi(t)]/\partial t \times \phi_j(x,t)$ where $\psi(t)$ is independent of x and taken to vanish when $t = 0$. We can then rewrite Eq. (2) as $\partial \ln\phi_j(x,t)/\partial t = \partial[-sx^2t + 2sxtF_j(t) + \psi(t)]/\partial t$ and this has the solution

$$\phi_j(x,t) = \exp[-sx^2t + 2sxtF_j(t) + \psi(t)]\phi_j(x,0). \tag{17}$$

Using the fact that $\phi_j(x,t)$ is normalised to unity for all t, yields $1 = \int\exp(-sx^2t + 2sxtF_j(t) + \psi(t))\phi_j(x,0)\,\mathrm{d}x$. We use this last result to eliminate $\exp(\psi(t))$ from Eq. (17) and obtain a result equivalent to Eq. (3) of the main text.

Appendix B

In this appendix, we derive the exact solution to Eq. (2) when distributions of allelic effects, at all loci, are initially Gaussian. We then extend the analysis to include the leading effects of the asymmetry of Eq. (4).

When the distributions of allelic effects at all loci are initially Gaussian, we take $\phi_j(x,0)$ to be given by $\phi_{j0}(x,0) = (2\pi\sigma_j^2)^{-1/2}\exp(-(x-a_j)^2/(2\sigma_j^2))$. Substituting this into Eq. (3) yields a Gaussian distribution for $\phi_j(x,t)$ whose variance is $\sigma_j^2/(1+2s\sigma_j^2 t)$ and whose mean is

$$\bar{x}_{j,0}(t) = \frac{a_j + 2s\sigma_j^2 t F_j(t)}{1 + 2s\sigma_j^2 t}, \tag{18}$$

where $F_j(t)$ is evaluated at the function $\bar{x}_{j0}$, i.e. $F_j(t) = \frac{1}{t}\int_0^t (\bar{x}_{j,0}(u) - \left[2\sum_{k=1}^n \bar{x}_{k,0}(u) - G(u)\right])\,\mathrm{d}u$. On differentiating Eq. (18) with respect to t, we quickly find a result equivalent to Eq. (8) of the main text.

To incorporate the asymmetry of Eq. (4) we define an average, denoted by $\langle\cdots\rangle_j$, so that for any function $g(x)$ $\langle g(x)\rangle_j = \int g(x)\mathrm{e}^{-st[x-F_j(t)]^2}\phi_{j0}(x,0)\,\mathrm{d}x / \int \mathrm{e}^{-st[x-F_j(t)]^2}\phi_{j0}(x,0)\,\mathrm{d}x$. We also introduce the function $f_j(x) = 1 + \varepsilon_j(x-a_j)^2\,\mathrm{sgn}(x-a_j)/(2\sigma_j^2)$ where $\mathrm{sgn}(x)$ denotes the 'sign' of x and takes the values ± 1 when $x \gtrless 0$. Then using Eqs. (3) and (5), we can write $\overline{x_j^r} = \int x^r\phi_j(x,t)\,\mathrm{d}x \simeq \langle x^r f_j(x)\rangle_j / \langle f_j(x)\rangle_j = \langle x^r\rangle_j + \varepsilon_j\psi_{rj} + \mathrm{O}(\varepsilon_j^2)$ where $\psi_{rj} \equiv \psi_{rj}(\langle x\rangle_j) = \{\langle x^r(x-a_j)^2\,\mathrm{sgn}(x-a_j)\rangle_j - \langle x^r\rangle_j\langle(x-a_j)^2\,\mathrm{sgn}(x-a_j)\rangle_j\}/(2\sigma_j^2)$.

To determine the moments of interest, we require the functions ψ_{1j}, ψ_{2j} and ψ_{3j}, and these can be straightforwardly obtained, using a computer algebra system (such as Maple$^{\mathrm{TM}}$), and are not given here.

The mean allelic effect, $\bar{x}_j$, follows from solution of $\bar{x}_j = \langle x\rangle_j + \varepsilon_j\psi_{1j}$. Note that generally, $\bar{x}_j$ depends not only on ε_j but also on ε_k for $k \neq j$. However, to zeroth order in asymmetry parameters (i.e. the ε_k), the mean allelic effect follows by simply setting all ε's to zero in $\bar{x}_j = \langle x\rangle_j + \varepsilon_j\psi_{1j}$ with the result $\bar{x}_{j,0} = \langle x\rangle_{j,0}$. In setting all ε's to zero, we must remember that $\langle x\rangle_j$ depends on $F_j(t)$, which, in turn depends on $\bar{x}_j$ and $\overline{G}$, and these latter quantities must also have all ε's set to zero. The solution for $\bar{x}_{j,0}$ obeys Eq. (8) of the main text.

To determine the mean allelic effect to first order in asymmetry parameters requires a substantially more complicated calculation; it is necessary to expand both the left and right hand sides of $\bar{x}_j = \langle x\rangle_j + \varepsilon_j\psi_{1j}$ to linear order in all asymmetry parameters (i.e. to linear order in all ε_k). While such a calculation can be explicitly carried out, details are not given here.

The variance in allelic effects, $\overline{(x_j - \bar{x}_j)^2} = \langle x^2\rangle_j - \langle x\rangle_j^2 + \varepsilon_j[\psi_{2j} - 2\langle x\rangle_j\psi_{1j}] + \mathrm{O}(\varepsilon_j^2)$ and with $\Lambda_j = (1 + 2s\sigma_j^2 t)^{-1}$, we obtain $\overline{(x_j - \bar{x}_j)^2} = \sigma_j^2\Lambda_j - \varepsilon_j\sigma_j^2\Lambda_j^2\,\mathrm{erf}\left((a_j - \langle x\rangle_j)/\sqrt{2\sigma_j^2\Lambda_j}\right) + \mathrm{O}(\varepsilon_j^2)$ where $\mathrm{erf}(\bullet)$ denotes the error function [15]. Since $\sigma_j^2\Lambda_j$ is independent of the ε's we can read off the part of the variance that is of zeroth order in ε.

The third central moment of allelic effects is $\overline{(x_j - \bar{x}_j)^3} = \varepsilon_j[\psi_{3j} - 3\langle x^2\rangle_j\psi_{1j} - 3\psi_{2j}\langle x\rangle_j + 6\langle x\rangle_j^2\psi_{1j}] + \mathrm{O}(\varepsilon_j^2)$ (the combination of terms: $\langle x^3\rangle_j - 3\langle x^2\rangle_j\langle x\rangle_j + 2\langle x\rangle_j^3$ is identically zero and hence absent from $\overline{(x_j - \bar{x}_j)^3}$, because $\langle\cdots\rangle_j$ is an average with respect to a Gaussian distribution). Evaluating all ψ_{rj} in the expression for $\overline{(x_j - \bar{x}_j)^3}$ at $\langle x\rangle_{j,0}$ yields an explicit expression for this moment that is correct to linear order in ε and is given by Eq. (9) of the main text.

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