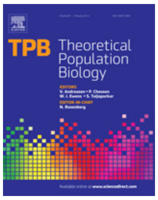
Theoretical Population Biology 99 (2015) 1–6

Contents lists available at ScienceDirect

Theoretical Population Biology

journal homepage: www.elsevier.com/locate/tpb



The probability of improvement in Fisher's geometric model: A probabilistic approach

Yoav Ram*, Lilach Hadany

The Department of Molecular Biology and Ecology of Plants, The George S. Wise Faculty of Life Sciences, Tel-Aviv University, Tel-Aviv 69978, Israel

HIGHLIGHTS

- We use a probabilistic approach to derive the probability of improvement in Fisher's geometric model of adaptation.
- Our approach provides an alternative interpretation of the main result of the model in terms of the model's parameters.
- This probabilistic approach can be used to solve additional problems in Fisher's geometric model.

ARTICLE INFO

Article history:
Received 15 June 2014
Available online 26 October 2014

Keywords:
Mathematical models
Fitness landscape
Mutations
Population genetics

ABSTRACT

Fisher developed his geometric model to support the *micro-mutationalism* hypothesis which claims that small mutations are more likely to be beneficial and therefore to contribute to evolution and adaptation. While others have provided a general solution to the model using geometric approaches, we derive an equivalent general solution using a probabilistic approach. Our approach to Fisher's geometric model provides alternative intuition and interpretation of the solution in terms of the model's parameters: for mutation to improve a phenotype, its relative beneficial effect must be larger than the ratio of its total effect and twice the difference between the current phenotype and the optimal one. Our approach provides new insight into this classical model of adaptive evolution.

1. Introduction

Fisher's geometric model (FGM) is a widely used model of adaptive evolution in which selection and mutation act on a combination of quantitative traits. Each trait has an optimal value, and the fitness of trait combinations is a decreasing function of the distance to the optimal trait combination. The model was originally used by Fisher to calculate the probability that a pleiotropic mutation – one that affects multiple traits – leads to an improved phenotype. In support of the *micro-mutationalism* hypothesis, Fisher found that small mutations are more likely to be beneficial and therefore contribute to adaptation and evolution (Fisher, 1930, p. 40; Waxman and Welch, 2005).

FGM is very relevant to both theoretical and experimental research in evolutionary biology. FGM has been used to infer distributions of fitness effects and fitness landscapes (Blanquart et al., 2014; Hietpas et al., 2013; MacLean et al., 2010; Melnyk and Kassen, 2011; Orr, 1998; Sousa et al., 2012; Trindade et al., 2012; Weinreich and Knies, 2013). Perfeito et al. (2014) followed the adaptation of 23 lines of *E. coli* and used Approximate Bayesian Computation to fit the data to the parameters of FGM, including the genomic mutation rate, number of traits, and the mean phenotypic effect of mutations. Bank et al. (Bank et al., 2014) estimated the distribution of fitness effects of 560 point mutations in *Hsp90* in *Saccharomyces cerevisiae* in six environments. Their results agree with predictions of the FGM. FGM was also used to test the *micro-mutationalism* hypothesis (Burch and Chao, 1999) and for analyzing evolutionary dynamics with simulations (Matuszewski et al., 2014; Venkataram et al., 2013). It has been extended to include fixation probabilities, fitness functions, and epistasis (Martin and Lenormand, 2008, 2006; Waxman, 2006). Finally, a recent article by Martin (2014) provides a biological justification for FGM by demonstrating its emergence in complex phenotypic networks.

Previous derivations of the probability of improvement in FGM used geometric approaches (Hartl and Taubes, 1996; Rice, 1990). Here, we study this problem using a probabilistic approach. Our result provides an alternative interpretation of how the probability of improvement in the phenotype after occurrence of a mutation is affected by the model's parameters: the total effect of mutation on phenotype, the number of affected traits, and the difference between the current phenotype and the optimal one. Additionally,

---

* Corresponding author.
E-mail address: yoavram@post.tau.ac.il (Y. Ram).

http://dx.doi.org/10.1016/j.tpb.2014.10.004
0040-5809/

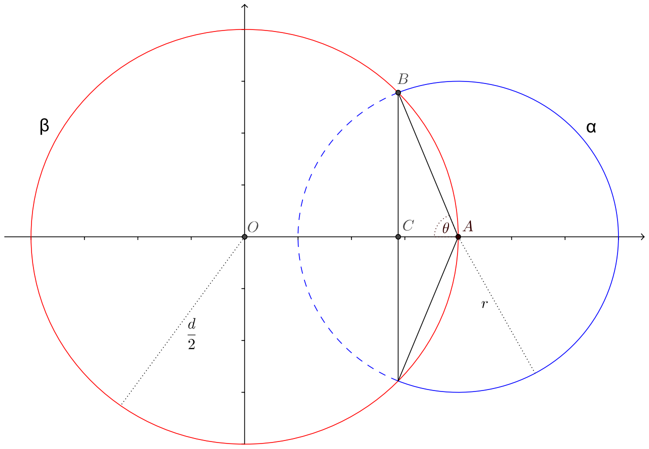


Fig. 1. *Two dimensional presentation of Fisher's geometric model.* The probability of improvement is the probability that a mutation changes the current phenotype A to a fitter phenotype that is closer to the optimum O. This probability is equal to the fraction of circle α that is inside the circle β (the dashed arc), because the circle α contains all the phenotypes that can be reached by a single mutation in A and the circle β contains all the phenotypes that are as fit as A.

we demonstrate how our approach can be used to analyze other properties of adaptation in FGM.

2. Model

We start by describing the general FGM. Then we review previously published results of the probability for improvement with two and three traits, with an arbitrary number of traits, and with a large number of traits.

2.1. Overview

In the following, we use the notation introduced by Fisher (1930, p. 40). In FGM, a phenotype is defined by n traits and therefore can be described by a vector in an n-dimensional space ($\mathbb{R}^n$). Because we are interested in the effect of mutation on phenotype, we define the Euclidean distance of the current phenotype from the optimal phenotype to be $d/2$. Without loss of generality, we assume that the optimal trait combination is $O = (0, \dots, 0)$ and the current phenotype is $A = (d/2, 0, \dots, 0)$. The effect of mutation on the current phenotype is given by a vector of magnitude r and a random direction.

Fisher's goal was to calculate the probability p that a mutation is beneficial—that is, that a mutation creates a mutant phenotype which is closer to the optimal phenotype than the current one.

2.2. Review of previous results

2.2.1. Two traits

Fig. 1 illustrates the model for two traits. We denote the current phenotype by $A = (d/2, 0)$. Phenotypes that can be reached by a single mutation of size r lie on circle α (centered at A with radius r). Phenotypes that are as fit as A are marked by circle β (centered at the origin with radius $d/2$). For a mutation to be beneficial, the mutant phenotype must be in the part of the circle α that is inside circle β (the dashed arc).

The two circles intersect at $B = (x, y)$ and $(x, -y)$ and we define $C = (x, 0)$. x is calculated using the two circle equations:

$$\begin{cases} \left(x - \frac{d}{2}\right)^2 + y^2 = r^2 \\ x^2 + y^2 = \left(\frac{d}{2}\right)^2 \end{cases} \Rightarrow$$

$$\begin{cases} x = \frac{d}{2} - \frac{r^2}{d} \\ y = \pm\sqrt{r^2 - \frac{r^4}{d^2}}. \end{cases}$$

Therefore, the length of AC is r^2/d. AB is the radius of circle α with length r, and θ is the angle between CA and AB. Therefore, $\cos\theta = AC/AB = r/d$. The probability of improvement p is the ratio between the (dashed) arc of circle α that lies inside circle β (with an angle 2θ) and the whole circle (with an angle 2π). For this two-dimensional case, the final formula for the beneficial mutation probability is (Rice, 1990)

$$p_2 = \frac{1}{\pi}\cos^{-1}\left(\frac{r}{d}\right),$$

where $\cos^{-1} x$ is arccos, the inverse function of cosine.

2.2.2. Three traits

With three traits, we have two spheres: sphere β, centered at $O = (0, 0, 0)$ with radius $d/2$, and sphere α centered at $(d/2, 0, 0)$ with radius r.

The intersection of these spheres defines a plane that cuts the sphere α to create a spherical cap. The area of this spherical cap has a simple formula, $2\pi rh$, where h is the height of the cap (equivalent to $r - AC$ in Fig. 1). This height can be found by the same way as in the two trait case: $h = r(1 - r/d)$.

Because the entire area of the surface of sphere α is $4\pi r^2$, the ratio between the area of the spherical cap and the whole sphere is (Fisher, 1930, p. 40)

$$p_3 = \frac{2\pi r^2\left(1 - \frac{r}{d}\right)}{4\pi r^2} = \frac{1}{2}\left(1 - \frac{r}{d}\right).$$

2.2.3. Arbitrary number of traits

In the general case of n traits there are two $n - 1$ hyperspheres, but the rest of the details are similar to the $n = 2, 3$ cases. Rice (1990) presented a solution based on an argument similar to that made in the three trait case on spherical caps:

$$p_n^R = \frac{\int_0^{\cos^{-1}\left(\frac{r}{d}\right)} \sin^{n-2}(\theta)d\theta}{\int_0^{\pi} \sin^{n-2}(\theta)d\theta}.$$

This result was also derived by others (Hartl and Taubes, 1996; Waxman and Welch, 2005). For $n = 2$ this becomes

$$\frac{\int_0^{\cos^{-1}\left(\frac{r}{d}\right)} 1d\theta}{\int_0^{\pi} 1\,d\theta} = \frac{1}{\pi}\cos^{-1}\left(\frac{r}{d}\right) = p_2.$$

For $n = 3$, this becomes

$$\frac{\int_0^{\cos^{-1}\left(\frac{r}{d}\right)} \sin(\theta)d\theta}{\int_0^{\pi} \sin(\theta)d\theta} = \frac{-\cos\left(\cos^{-1}\left(\frac{r}{d}\right)\right) + \cos(0)}{-\cos(\pi) + \cos(0)}$$
$$= \frac{1}{2}\left(1 - \frac{r}{d}\right) = p_3.$$

Kimura (1983, p. 137) presented a different formula (which is equivalent, see below):

$$p_n^K = \frac{1}{2} I_{1-\frac{r^2}{d^2}}\left(\frac{n-1}{2}, \frac{1}{2}\right),$$

where $I_x(a, b)$ is the regularized incomplete beta function. He did not provide a derivation for this result.

2.2.4. Large number of traits

Fisher presented an asymptotic result for a large number of traits (Fisher, 1930, p. 40), which is very elegant due to the use of