Theoretical Population Biology 104 (2015) 59–67

Contents lists available at ScienceDirect

Theoretical Population Biology

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

On the interpretation and relevance of the Fundamental Theorem of Natural Selection

Warren J. Ewens[a,*], Sabin Lessard[b]

[a] Department of Biology, The University of Pennsylvania, Philadelphia, PA 19104, USA
[b] Département de mathématiques et de statistique, Université de Montréal, Montréal, Québec H3C 3J7, Canada

ARTICLE INFO

Article history:
Received 18 February 2015
Available online 26 July 2015

Keywords:
Average effects
Average excesses
Fitness
Gene frequencies
Genic evolutionary potential
Mean fitness

ABSTRACT

The attempt to understand the statement, and then to find the interpretation, of Fisher's "Fundamental Theorem of Natural Selection" caused problems for generations of population geneticists. Price's (1972) paper was the first to lead to an understanding of the statement of the theorem. The theorem shows (in the discrete-time case) that the so-called "partial change" in mean fitness of a population between a parental generation and an offspring generation is the parental generation additive genetic variance in fitness divided by the parental generation mean fitness. In the continuous-time case the partial rate of change in mean fitness is equal to the parental generation additive genetic variance in fitness with no division by the mean fitness. This "partial change" has been interpreted by some as the change in mean fitness due to changes in gene frequency, and by others as the change in mean fitness due to natural selection. (Fisher variously used both interpretations.) In this paper we discuss these interpretations of the theorem. We indicate why we are unhappy with both. We also discuss the long-term relevance of the Fundamental Theorem of Natural Selection, again reaching a negative assessment. We introduce and discuss the concept of genic evolutionary potential. We finally review an optimizing theorem that involves changes in gene frequency, the additive genetic variance in fitness and the mean fitness itself, all of which are involved in the Fundamental Theorem of Natural Selection, and which is free of the difficulties in interpretation of the Fundamental Theorem of Natural Selection.

1. Introduction

The Fundamental Theorem of Natural Selection (FTNS) as now understood is very general. It is a "whole genome" result in the sense that in the theorem the fitness of any individual is allowed to depend, in an unspecified way, on its autosomal genomic makeup. (The sex chromosomes are also ignored in the FTNS.) It also holds for any form of mating, random or otherwise. Since the theorem concerns the effect of natural selection only, no mutations are allowed. Various simplifications are made in the statement of the theorem. For example, despite the fact that the FTNS relates to diploid populations, no account is taken in the theorem as presented by Fisher of the existence of two sexes, with possibly different fitness values for any genotype between the two sexes. Next, in effect an infinitely large population is assumed so that no random changes in gene frequency are allowed. Various other simplifications are made, no doubt of necessity, and a completely general theorem awaits development. The same simplifying assumptions that are made in the FTNS will also be made in this paper.

There are various versions of the FTNS. Different versions make different assumptions about "time" and about "fitness". Concerning "time", there are both discrete-time and continuous-time versions of the FTNS, and within these two there are various subdivisions, some still under investigation. Concerning fitness, in the general literature the fitness of any individual is sometimes taken as a parameter determined by that individual's genotype, and sometimes (for example Price, 1970) as the actual number of offspring that individual has (or perhaps half that number in the diploid case). Since the FTNS is a deterministic result in which the population size is taken as infinite, in the discussion of the FTNS in discrete time with non-overlapping generations there is no effective difference between these two definitions, and to be concrete we here use the parameter definition of fitness in this context. Moreover, we assume that for each genotype this parameter does not depend on time and population state.

Fisher's (1958) statement of the FTNS, namely "The rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time" is nowadays understood

---

* Corresponding author.
E-mail address: wewens@sas.upenn.edu (W.J. Ewens).

http://dx.doi.org/10.1016/j.tpb.2015.07.002

as stating that "The partial rate of change in the mean fitness of any population at any time is equal to the additive genetic variance in fitness in that population at that time". The meaning of the words "partial change " is discussed later, and it is plausible that by using the word "increase" rather than "change" Fisher implied by "increase" the same meaning as "partial change".

Fisher's statement clearly refers to a continuous-time process. For simplicity we consider instead a discrete-generation process in which, at discrete time points 1, 2, 3, . . . , a parental generation gives birth to an offspring generation and then dies. However, the conclusions reached can be extended to models with overlapping generations in continuous time as well as discrete time (see, e.g., Ewens, 1989, Lessard, 1997 and Grafen, 2015). Unless indicated otherwise when discussing this discrete-time case, all measurements are taken at the time of conception of any generation and the word "change" means the change in the quantity considered between parental and offspring generations values at their respective times of conception.

2. Background

Despite previous discussion on the total change in mean fitness (see, e.g., Kempthorne, 1957 and Kimura, 1958), the interpretation of the FTNS remained largely unclear until Price's (1972) analysis. Price's analysis was, at least initially, presented in discrete time although, because he was attempting to validate Fisher's continuous-time result given above, his wording had a continuous-time flavor. Price's analysis is based on a partial change which he denoted $\partial_{NS}\bar{w}$ and which is defined in Eq. (11) in a context of discrete non-overlapping generations. (We have changed Price's M to $\bar{w}$, the modern notation for a mean fitness.) Price's equation (2.7) states that $\partial_{NS}\bar{w}$ is a change in mean fitness between discrete time points and his concluding statement of the theorem (his Eq. (5.14)) involves this change. Thus it can be argued that Price's analysis, despite much of his wording, relates to a discrete-time process. However in melding his result with Fisher's verbal presentation he does not give the discrete-time result presented in Eq. (13).

As discussed below the FTNS is quintessentially a diploid population result, and the entire analysis of the FTNS given below assumes a diploid population. The FTNS depends, in the diploid case, on the concept of the average effect of an allele on fitness, and it is convenient to discuss this concept briefly. There are in fact two average effect concepts, and Fisher (1958, p. 35) confusingly uses both without any clarification. What has been called the α definition (Ewens, 2010) is that the average effects are found by minimizing

$$\sum_g P_g \left\{ w_g - \bar{w} - \left(\sum_{i,j \text{ in } g} \alpha_{ij} \right) \right\}^2 \tag{1}$$

with respect to the α_{ij} values. The inner sum in (1) is sometimes called the "breeding value" of genotype g, and for convenience we denote it by α_g. In the above expression g indexes whole genome genotypes, P_g is the frequency of whole-genome genotype g and w_g is the fitness of this genotype, that is its viability from the time of conception to the time of reproduction, which is assumed to be time- and frequency-independent. Moreover,

$$\bar{w} = \sum_g P_g w_g \tag{2}$$

is the population mean fitness (henceforth simply "mean fitness") and α_{ij} is the "α" version average effect of allele j at gene locus i. In the expression (1) the inner sum is taken over all alleles at all loci in genome, with, for each whole-genome genotype g, α_{ij} occurring once, twice or not at all in the inner sum depending on whether allele j at gene locus i occurs once, twice or not at all in that genotype. The outer sum is then taken over all whole-genome genotypes. These average effects are also required to satisfy the constraint that for each gene locus i,

$$\sum_j \alpha_{ij} p_{ij} = 0, \tag{3}$$

where p_{ij} is the frequency of allele j at gene locus i. (Thus at gene locus "i" the sum $\sum_j p_{ij}$ of the frequencies of the various possible alleles is 1.)

On the other hand, the β definition average effects (Ewens, 2010) are found by minimizing

$$\sum_g P_g \left\{ w_g - \left(\sum_{i,j \text{ in } g} \beta_{ij} \right) \right\}^2 \tag{4}$$

with respect to the β_{ij} values. The inner sum in (4) is sometimes called the "additive genetic value" of genotype g, and for convenience we denote it by β_g. The symbols and summations in this expression have the same meaning as in (1). The additive genetic value of genotype g can be interpreted as the fitness of g as best predicted from the alleles in g counted as many times as they occur. The relation between the α_{ij} values and the β_{ij} values is that for each allele j at each locus i,

$$\beta_{ij} = \alpha_{ij} + \frac{\bar{w}}{2K}, \tag{5}$$

where K is the number of loci in the genome that influence fitness. (From now on, only those loci are considered. The factor 2 arises because all loci are diploid.) There is a constraint on the β_{ij} values, namely

$$\sum_j \beta_{ij} p_{ij} = \frac{\bar{w}}{2K} \tag{6}$$

for each gene locus i, which derives from the constraint (3) on the α_{ij} values.

It is in general very difficult to find explicit expressions for average effects, but fortunately explicit expressions are not needed for the discussion in this paper. For some purposes one definition of average effects is more convenient and for other purposes the other definition is more convenient. Under both definitions the average effects of the various alleles usually depend on their frequencies (an exception will be given in Example 1 below) and thus in general average effects will change from one generation to the next as these frequencies change. This is a central observation when discussing the FTNS.

The whole genome "additive genetic variance" in fitness, denoted here and throughout by σ_A^2, is the sum of squares removed by fitting the α parameters in (1) or, equivalently, the β parameters in (4). Under the constraint (3), we have

$$\sigma_A^2 = \sum_g P_g \alpha_g^2 = \sum_g P_g \left(\sum_{i,j \text{ in } g} \alpha_{ij} \right)^2. \tag{7}$$

It is not easy to write down an explicit formula for σ_A^2, but (as with the average effects) an explicit expression is not necessary for the purposes of this paper.

The population mean fitness $\bar{w}$ in some given parental generation at its time of conception can be expressed via the β definition of average effects instead of the actual genotypic fitnesses in the two equivalent forms

$$\bar{w} = \sum_g P_g \beta_g = 2 \sum_i \sum_j p_{ij} \beta_{ij}, \tag{8}$$