



Review **Comparative research progress of quantitative traits and neutral marker differentiation**

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Abstract: The relative roles of natural selection and random genetic drift in explaining amongpopulation divergence have been assessed through comparative studies of quantitative genetic across populations (Qst) and neutral marker differentiation (Fst). The Qst-Fst comparison can provide attention to two crucial but understudied issues in evolutionary genetics: What role do random genetic drift and directed natural selection play in population differentiation of quantitative traits? 2) Is there a relationship between the degree of differentiation of neutral marker loci and the degree of differentiation of genes encoding quantitative traits? The essential principles, function, practical application, and quantitative substitute of quantitative inheritance and neutral marker distinction between natural populations are described in this review, which provides a theoretical foundation for solving a variety of problems in evolution and ecological genetics.

Keywords: Quantitative character; Neutral molecular markers; Phenotypic differentiation

1. Introduction

The majority of plant and animal species, including humans, are subdivided into numerous partially isolated subspecies. Under the impact of regional and temporal heterogeneity on the selection of genetic features, subspecies eventually differentiate genetically and phenotypically, according to the benefits of natural selection, genetic drift, migration, and mutation (Leinonen et al., 2010; 2013). Humans, like most other plant and animal species, are separated into a myriad of largely isolated subspecies. Subspecies eventually diversify genetically and phenotypically under the pressure of spatial and temporal heterogeneity on genetic trait selection, owing to the benefits of natural selection, genetic drift, migration, and mutation (Leinonen et al., 2010; 2013). The relative role of genetic drift and natural selection as causes of quantitative trait differentiation in populations is uncertain, despite substantial breakthroughs in the study of phenotypic plasticity and its well-documented importance in adaptation and evolution (Kelly et al., 2012; Sommer, 2020). There have been statistical tests established for quantitative features with zero expectations utilizing neutral differentiation as a natural selection test, but they are not commonly employed (Leinonen et al., 2010). It's likely that using field data forces you to make assumptions about unknown populations, such as mutation rates, time since divergence, and population size (Merilä and Crnokrak, 2001). Comparing genetic divergence between neutral marker loci and quantitative traits is one way to analyze the relative impact of genetic drift and natural selection as drivers of genetic variation between populations with quantitative traits (Leinonen et al., 2010; Gilbert and Whitlock, 2015).

Comparison of quantitative trait across populations (Qst) and differentiation at neutral molecular markers (Fst), Qst-Fst comparison provides a means for researchers to distinguish natural selection from genetic drift as the cause of population differentiation of complex polygenic traits (Brommer, 2011). Fst is the traditional basic index to measure population genetic differentiation and population inheritance, which is widely used in the field of genetics (Leinonen et al., 2013).

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Copyright: © 2022 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/). Qst refers to the differences of quantitative traits among populations under the effects of genetic drift, selection, gene flow and environmental adaptability (Brommer, 2011). When Qst > Fst, which studies genetic differences in traits encoding beyond what would be expected on a drift basis, suggests that natural selection favours different phenotypes in different populations. When Qst = Fst, it cannot be ruled out that the observed differentiation is caused by genetic drift alone. When Qst < Fst, the same phenotype is favored in different populations and stable selection occurs (Figure 1) (Brommer, 2011). Understanding the causes and consequences that influence this differentiation has important implications for the biological sciences, including basic research, such as evolutionary biology, ecology and genetics, and applied fields, such as forestry and fisheries management, medical biology (Leinonen et al., 2013). In particular, it is possible to determine whether population differentiation is caused by a process of natural selection or by a process of neutral inheritance. Therefore, the measurement of Qst associated with neutral differentiation is an important study applicable to both evolutionary and conservation biology. However, many species, especially endangered species, are unable to complete the breeding experiments required to calculate their narrow or broad Qst. At present, a large number of studies replace Qst with phenotypic divergence in a trait (Pst) (Leinonen et al., 2006; Zhou et al., 2012). Quantification of Pst is based on phenotypic measurements of traits of several individuals in multiple populations in the wild (Brommer, 2011). In order to provide a theoretical foundation for understanding the mechanisms underlying phenotypic differentiation, the essential principles, function, practical application, and quantitative substitute of quantitative inheritance and neutral marker distinction between natural populations are described in this review.



Figure 1 The Qst/Pst and Fst comparisons

2. Non-metric phenotypic traits

The previous methods for investigating the effects of natural selection and random genetic drift on phenotypes were based on a simple quantitative genetics formula and a population genetics method to establish the theory of natural selection and random genetic drift on population average phenotype evolution (Wójcik et al., 2006). Also, regardless of their complexity, employ landmarks or contours in two or three dimensions. Directional, stable, and random selection were simulated in the variation space defined by the principal component of the phenotypic covariance matrix based on population-level estimation of phenotypic covariance (Leinonen et al., 2013). Non-metric characteristic analysis revealed significant selectivity in mandible size, mandible shape, and skull shape in the population of yellow-necked rats (*Apodemus flavicollis*) (Wójcik et al., 2006), and the

evolutionary pattern of shrew molar morphology may be a selection with varying intensity and orientation (Leinonen et al., 2013).

3. Comparison of quantitative and neutral marker differentiation

3.1 Differences in quantitative traits and neutral molecular markers

A comparison of quantitative attributes and neutral marker differentiation aids in evaluating the relative contributions of natural selection and random genetic drift in explaining population variation (Leinonen et al., 2010; 2013). In various species, quantitative features are compared across populations and differentiation at neutral molecular markers is used (Fst). According to the results of the Qst-Fst comparison (Leinonen et al., 2010; 2013; Merilä and Crnokrak, 2001; Brommer, 2011), natural selection is the primary cause of quantitative trait differences. The variance in quantitative traits between populations as a result of genetic drift, selection, gene flow, and the environment is referred to as Qst = $\sigma^2 GB/(\sigma^2 GB+2\sigma^2 GW)$, where $\sigma^2 GB$ and $\sigma^2 GW$ are additive genetic variants within and within populations that are unaffected by maternal, environmental, or non-additive genetic effects (Marin et al., 2020). Fst is a conventional basic metric for determining population genetic difference and consequences. The expected degree of difference between populations of genetic drift and gene flow can be estimated by estimating the degree of divergence between populations of neutral marker loci. Three methods are typically used to calculate Fst: genetic differentiation coefficient (Gst), RST (Merilä and Crnokrak, 2001; Brommer, 2011). Where Vb represents intragroup variance and Vw represents intergroup variation, Fst = Vb/(Vb+Vw). Higher gene flow impedes local adaptation and homogenizes the gene pool in populations with lower Fst values, whereas genetic drift in populations with higher Fst values shifts the mean value of characteristics relatively freely and randomly, resulting to population divergence (Leinonen et al., 2009).

3.2 Comparison of quantitative traits and neutral molecular markers.

There are three possible results in the comparison of Qst and Fst: If Qst > Fst, the differentiation degree of quantitative traits exceeds that of simple genetic drift. Therefore, phenotypic differentiation must be driven by directional natural selection conducive to different phenotypes in different populations; 2) If Qst = Fst, the observed differentiation degree of quantitative traits can be obtained only through genetic drift, but it cannot be said that the differentiation degree is caused by genetic drift, but the influence of drift and selection cannot be distinguished; 3) If Qst Fst, the same phenotype is preferred in different populations and stable selection occurs (Leinonen et al., 2010; 2013; Merilä and Crnokrak, 2001; Brommer, 2011). There are three possible results in the comparison of Qst and Fst: If Qst > Fst, the differentiation degree of quantitative traits exceeds that of simple genetic drift. Therefore, phenotypic differentiation must be driven by directional natural selection conducive to different phenotypes in different populations; 2) If Qst = Fst, the observed differentiation degree of quantitative traits can be obtained only through genetic drift, but it cannot be said that the differentiation degree is caused by genetic drift, but the influence of drift and selection cannot be distinguished; 3) If Qst Fst, the same phenotype is preferred in different populations and stable selection occurs (Leinonen et al., 2010; 2013; Merilä and Crnokrak, 2001; Brommer, 2011). Through Qst and Fst comparison, genomics can be linked with ecology and morphology, and the functional relationship from genotype to phenotype, from phenotype to adaptation, and reproductive separation can also help us solve two important problems: 1) What is the relative importance of random genetic drift and directional natural selection on population differentiation of quantitative traits? 2) Does the degree of differentiation of neutral marker loci predict the degree of differentiation of genes encoding quantitative traits? (Mckenna et al., 2010; Leinonen et al., 2006).

It has practical implications for solving problems related to evolution and ecological genetics (Leinonen et al., 2010), including basic research fields such as evolutionary biology, ecology, and genetics, as well as application fields such as forestry and fishery management, and medical biology (Leinonen et al., 2013), particularly to determine whether population differentiation is caused by natural selection or a neutral genetic process (i.e., genetic drift). 2001 and 2010, 20 studies included 17 species (including 10 plants, 4 invertebrates, and 3 vertebrates) and 77 studies included 50 species (including 27 plants, 12 invertebrates, 10 vertebrates, and 2 fungi). For meta-analysis, the traits were split into morphological qualities, life history traits, and behavioral traits. Life history traits are those that are directly associated to fitness, such as growth rate and fecundity, while morphological features are those that are measured measurements, such as bone size (Leinonen et al., 2010). Different neutral markers, including as restriction fragment length polymorphism (RFLP), random amplified polymorphic DNA (RAPD), expressed sequence tag (Estp), and cleaved amplified polymorphic sequences, were found to have statistical significance (CAPS). The Fst results of AFLP were similar, however the difference between the Qst and Fst of allozyme markers was significantly bigger than the difference between the Qst and Fst of DNA gene markers. The average Ost of most species is greater than Fst, indicating that life history traits are stably inherited while morphological traits are biased to be driven by natural selection; there is a significant positive correlation between the population differentiation index of Qst and Fst, indicating that neutral marker differentiation can predict quantitative trait genetic differentiation; and there is a significant positive correlation between the population differentiation index of Qst and Fst, indicating that neutral marker differentiation can predict quantitative trait genetic differentiation. There is a strong positive correlation between Qst and Fst, which can be explained by a common component that causes the two to differ. The Fst of neutral marker genes often rises with distance, which could play a role. Increased distance may also increase the heterogeneity of selection pressure, resulting in a higher Qst. Increased distance may also increase the heterogeneity of selection pressure, resulting in a higher Qst. Another theory is that if gene flow between populations is constrained as a result of increased isolation induced by distance, drift will eventually lead to genetic differentiation of neutral regions (Leinonen et al., 2009; Morgan et al., 2005). The examples of applications of Qst-Fst comparisons were showed in Table 1 (Leinonen et al., 2013).

Context	Inference
Local adaptation	Identification of natural selection as a cause of broad-scale clinal variation in morphological and life-history traits.
Sexual selection	Identification of sex-specific selection as the cause of evolution of sexual dimorphism.
Speciation	Adaptive divergence maintains species integrity despite high gene flow.
Evolutionary stasis	Identification of selective constraints explaining phenotypic uni- formity across species ranges.
Human-induced evolu-	Demonstrations of how human-induced habitat changes can either
tion	cause or impair adaptation.

Table 1 The examples of applications of Qst-Fst comparisons (Leinonen et al., 2013)

Artificial selection	Demonstrations of how selective breeding shapes
	diversification and population structuring of crop species.
Conservation	Demonstrations that setting conservation priorities should not be
	based only on neutral marker diversity, and that Qst-Fst compari-
	sons can be used to identify populations that are suitable for
Management	translocation.
	Identification of units or populations that are suitable for translo-
	cation or stocking.
Transcriptomics	Identification of genes under selection using the
	distribution of Qst values of transcription levels.
Human evolution	Identification of adaptive phenotypic differentiation among hu-
	man populations.

3.3 Differences in phenotypic features and quantitative trait substitution between populations

Measuring Qst in the context of neutral differentiation is unquestionably significant research in evolutionary and conservation biology. Many species, particularly endangered species, are unable to complete the breeding trials necessary to compute their narrow or broad Qst, as well as gather the population quantitative genetic data needed to calculate Qst. Phenotypic variety in a characteristic (Pst) is commonly employed to replace Qst in fish (Storz, 2002), crustaceans (Zhou et al., 2012), amphibians (Alho et al., 2010), birds (Saether et al., 2007; Phillimore et al., 2008), and nursing animals (Wójcik et al., 2006). The phenotypic measurement of attributes of several individuals in several populations in the open environment is used to quantify Pst (Brommer, 2011). Pst = $c\sigma^2 B/(c\sigma^2 B+2h^2\sigma^2 W)$, where $\sigma^2 B$ = inter-population phenotypic variance, $\sigma^2 W$ = intra-population phenotypic variance, h^2 = heritability, and scalar c = additive genetic effects across populations (Raeymaekers et al., 2007). However, because it is impossible to predict the precise values of c and h^2 in a group of populations, the absence of accurate values of c and h^2 may cause Qst to be extremely close to zero, even if Pst is substantial. Researchers must carefully analyze various values of c and h^2 in order to compare Pst and Fst more correctly.

4. Summary and Prospect

To summarize, researchers can distinguish between natural selection and genetic drift as the sources of population differentiation of complex polygenic characteristics by comparing the differences between quantitative traits and neutral molecular markers across populations, i.e. the Qst-Fst comparison. Many endangered species, on the other hand, are unable to complete the breeding experiments required to establish their narrow or broad Qst. Pst is currently being used to replace Qst in a significant number of studies, but due to the lack of specific values for critical parameters, researchers must carefully analyze the various Pst values.

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