Genetics: Published Articles Ahead of Print, published on December 1, 2005 as 10.1534/genetics.105.050583

The effects of dominance, regular inbreeding and sampling design on Q_{ST}, an estimator of population differentiation for quantitative traits

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Running Head: Q_{ST} with dominance and inbreeding

Key words: population differentiation, quantitative genetics, genetic determinism, computer simulations, individual based model, variance components, neutral models

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Abstract

In order to test whether quantitative traits are under directional or homogenizing selection, it is common practice to compare population differentiation estimates at molecular markers (F_{ST}) and quantitative traits (Q_{ST}). If the trait is neutral and its determinism is additive, then theory predicts that $Q_{ST} = F_{ST}$, while $Q_{ST} > F_{ST}$ is predicted under directional selection for different local optima, and $Q_{ST} < F_{ST}$ is predicted under homogenizing selection. However, non additive effects can alter these predictions. Here, we investigate the influence of dominance on the relation between Q_{ST} and F_{ST} for neutral traits. Using analytical results and computer simulations, we show that dominance generally deflates Q_{ST} relative to F_{ST}. Under inbreeding, the effect of dominance vanishes, and we show that for selfing species, a better estimate of Q_{ST} is obtained from selfed families than half-sib families. We also compare several sampling design and found that it is always best to sample many populations (> 20) with few families (5) rather than few populations with many families. Providing that estimates of Q_{ST} are derived from individuals originating from many populations, we conclude that the pattern $Q_{ST} > F_{ST}$, and hence the inference of directional selection for different local optima, is robust to the effect of non additive gene actions.

INTRODUCTION

Understanding the evolutionary forces that shape ecologically important traits among populations of the same species is one of the central theme of evolutionary biology research (Merila and Crnokrak 2001). These forces are first selection, which can homogenize phenotypes across populations or on the contrary make them diverge because of different local optima, a phenomenon called local adaptation. But the other micro-evolutionary forces also affect quantitative traits. These forces are classically mutation, and particularly migration and random genetic drift. In the absence of selection, these last three forces are the only one acting on traits at least partly genetically determined (Lande 1992, Whitlock 1999, Hendry 2002). The same forces affect patterns of variation at molecular markers, hence the idea of comparing statistics obtained from molecular markers and quantitative traits. Lande (1992) and Whitlock (1999) showed that for a neutral trait with a strictly additive determinism, differentiation estimated from quantitative traits should be equal to that estimated from molecular markers. Spitze (1993), using results obtained by Wright (1951), derived a statistic for quantitative traits equivalent to Wright's F_{ST} (Wright 1969), statistics that he called Q_{ST}. Under strict neutrality and additivity, $Q_{ST} = F_{ST}$. Different local optima in different populations lead to $Q_{ST} > F_{ST}$, while selection for the same optimum across populations of the same species lead to $Q_{ST} < F_{ST}$ (Crnorkrak and Merila 2002, McKay and Latta 2002). These predictions for the relation between Q_{ST} and F_{ST} were confirmed using computer simulations by Le Corre and Kremer (2003) for both random mating and highly selfing situations.

Merila and Crnokrak (2001) and McKay and Latta (2002) have recently reviewed the empirical literature on comparisons between differentiation estimates obtained from quantitative traits and molecular markers. The general pattern that emerges from these reviews is that quantitative traits are on average more differentiated than molecular markers despite showing a very large variability.

While these reviews seem to confirm the ubiquitness of local adaptation, the conclusions

are based on the assumption that the quantitative traits have a purely additive determinism. Several authors have pointed out that it is crucial to investigate how Q_{ST} would behave in the presence of dominance and epistasis at quantitative traits (Whitlock 1999; Le Corre and Kremer 2003). Lynch *et al.* (1999) suggested that epistasis would drive Q_{ST} upwards. Whitlock (1999) demonstrated that additive by additive epistasis would on the contrary drive Q_{ST} downwards, and suggests that dominance could affect Q_{ST} in either way. Merila and Crnokrak (2001) and Yang *et al.* (1996) have also pointed out that inbreeding could affect the relation between Q_{ST} and F_{ST}.

Lopez-Fanjul *et al.* (2003) investigated the effect of dominance and epistasis, using a two loci, two alleles model. They concluded that with dominance, $Q_{ST} < F_{ST}$ for low to moderate frequency of the recessive alleles, and $Q_{ST} > F_{ST}$ otherwise. Epistasis diminished Q_{ST} relative to F_{ST}, unless the recessive alleles are very frequent. They therefore concluded that the comparison between Q_{ST} and F_{ST} should be restricted to purely additive traits. This would certainly be a strong limitation of this approach, as the genetic determinism of quantitative traits is seldom understood. They arrived at these conclusions by looking at the effect on allelic frequencies of a one generation bottleneck of size $N = 2$. However, several authors (Robertson 1952, Willis and Orr 1993, Cheverud and Routman 1996, Naciri-Graven and Goudet 2003, Barton and Turelli 2004) showed that bottlenecks affect strongly the additive variance within lines. It is thus difficult to conclude wether the pattern observed by Lopez-Fanjul *et al.* (2003) is general or specific to the situation where bottlenecks have occurred in the very recent past.

A second issue touched upon in Lopez-Fanjul *et al.* (2003) concerns the large errors in the estimation of F_{ST} and particularly Q_{ST}. This point was already noted in the early eighties by Rogers and Harpending (1983) who pointed out that "one polygenic character contains as much information about population relationships as one single-locus marker". As comparisons between Q_{ST} and F_{ST} depend critically on the variance of these statistics, it seems worthwhile to investigate which sampling scheme minimizes the variance of these esti-

mators. Sampling design issues have been addressed for F_{ST} (Pons and Petit 1995;Pons and Chaouche 1995), and O'Hara and Merila (2005) have recently investigated the statistical properties of Q_{ST}.

The goal of this paper is to characterize the effects of dominance and inbreeding on Q_{ST} in the absence of selection. We first obtain analytical results for the expression of Q_{ST} for a bi-allelic trait and identify situations in which Q_{ST} is expected to be larger than F_{ST}. As the analytical results are limited to bi-allelic loci, we use computer simulations to explore the effect that dominance and inbreeding have on Q_{ST}, using estimators of Q_{ST} based (i) on allele frequency and (ii) on covariance among relatives obtained from classical crossing designs in common garden experiments. We also explore how the variance of Q_{ST} is affected by the experimental design.

METHODS AND RESULTS

The quantities needed in order to obtain the expression for F_{ST} and Q_{ST} are the gene diversity within populations H_S, and overall H_T, the variance among populations V_B and the additive variance within populations, V_{AW}.

With these quantities, F_{ST} is defined as $1 - \frac{\overline{H_S}}{H_T}$ (Hartl and Clark 1997), while Q_{ST} is defined as:

$$Q_{ST} = \frac{(1+f)V_B}{(1+f)V_B + 2V_{AW}} \tag{1}$$

(Bonnin *et al.* 1996), where V_B is the among population component of variance for the trait, and V_{AW} the additive genetic variance within populations. The factor 2 associated with V_{AW} is due to the fact that for quantitative traits, genotypes are compared, while genes are compared when computing F_{ST} (Lynch and Spitze 1994).

Consider a locus with 2 alleles, A and B, with respective frequencies p_i and $q_i = 1 - p_i$ in population i . We will use the notation of Falconer (Falconer and MacKay 1996) for genotypic value. Under regular inbreeding, genotypic values and frequencies of the different

genotypes are given in table 1.

[Table 1 about here.]

Gene diversity within population H_S depends only on allelic frequencies. It writes:

$$H_{Si} = 2p_iq_i = 2(p_i - p_i^2).$$

Overall diversity H_T writes as:

$$H_T = 2\bar{p}\bar{q},$$

where $\bar{p} = \frac{\sum_{i=1}^{n} p_i}{n}$ is the average frequency of the recessive allele A.

F_{ST} is defined as:

$$F_{ST} = \frac{H_T - \overline{H_S}}{H_T} \tag{2}$$

The variance among populations of trait means, V_B is defined as:

$$V_B = \frac{1}{n}\sum M_i^2 - (\overline{M})^2$$

where M_i , the mean trait value in population i can be written $(q_i - p_i)a + 2p_iq_i(1-f)d$.

After replacement and simplifications, V_B becomes:

$$V_B = 2a^2(H_T - \overline{H_S}) - 4ad(1-f)Cov(p, H_S) + d^2(1-f)^2V(H_S) \tag{3}$$

While under pure additivity, V_B is proportional to $H_T - \overline{H_S}$ (and therefore to the first and second moments of allele frequencies), in the presence of dominance V_B becomes a complex function of higher moments of allele frequencies. The effect of dominance depends on allelic frequencies and gene diversity. When the recessive allele is frequent ($\bar{p} > 0.5$), the covariance term is negative and V_B increases compared to the case without dominance.

When the recessive allele is rare ($\bar{p} < 0.5$), V_B increases providing that $\beta(p, H_S) > \frac{d}{4a}$, where $\beta(p, H_S)$ is the slope of the regression of the frequency of the recessive allele on H_S.

Finally, we seek within population additive variance. For nl loci, additive variance is quantified as $V_A = 2\sum_{j=1}^{nl}\sum_{i=1}^{nk} p_{ij}e_{ij}\alpha_{ij}$ (LYNCH and WALSH 1998), where e_{ij} represents the average excess of allele i at locus j and α_{ij} the average effect of allele i at locus j. For one locus, following TEMPLETON (1987), we obtain:

$$\begin{aligned} e_A^i &= (p_i + q_i f)(-a - M_i) + q_i(1-f)(d - M_i) = (p_i + q_i f)(-a) + q_i(1-f)d - M_i \\ e_B^i &= (p_i(1-f)(d - M_i) + (q_i + p_i f)(a - M_i) = (p_i(1-f)d + (q_i + p_i f)a - M_i \\ \alpha_j^i &= e_j^i/(1+f),\ j \in (A, B) \end{aligned} \tag{4}$$

Expression for the additive variance within population i is then:

$$V_A^i = 2(p_i\alpha_A^i e_A^i + q_i\alpha_B^i e_B^i) = \frac{2}{1+f}(p_i(e_A^i)^2 + q_i(e_B^i)^2)$$

which, after replacement and simplifications gives:

$$\begin{aligned} V_A^i &= \frac{2p_iq_i}{(1+f)}\left[(1+f)a - (1-f)(q_i - p_i)d\right]^2 \\ V_A^i &= \frac{H_{Si}}{(1+f)}\left[(1+f)a - (1-f)(q_i - p_i)d\right]^2 \end{aligned}$$

For a number n of populations, the expression becomes:

$$V_{AW} = \frac{1}{n(1+f)}\sum_{i=1}^{n} H_{Si}\left((1+f)a - (1-f)(q_i - p_i)d\right)^2 \tag{5}$$

From this expression we see that dominance decreases the additive variance within populations when the recessive allele is rare ($p < 0.5$), while it increases it when the recessive

allele is frequent. This is easily understood since when the recessive allele is rare, it will be found mainly in heterozygote which do not differ much in phenotype from the dominant homozygote.

The expression for Q_{ST} is obtained by replacing V_{AW} and V_B in equation (1).

From equations (3) and (5), we see that inbreeding diminishes the contribution of dominance to both V_B and V_{AW}. Thus, as inbreeding increases, the effect of dominance on Q_{ST} diminishes, and, unless $d \gg a$, dominance will have little effect on Q_{ST} under strong inbreeding.

The expression of Q_{ST} for specific cases are listed below:

- No dominance, $\forall f$

  In the absence of dominance ($d = 0$), V_{AW} reduces to:

$$V_{AW} = \frac{a^2(1+f)^2}{n(1+f)} \sum H_{Si} = a^2(1+f)\overline{H_S}$$

  while V_B takes expression:

$$V_B = 2a^2(H_T - \overline{H_S}).$$

  and Q_{ST} becomes:

$$Q_{ST\,d\to 0} = \frac{2(1+f)a^2(H_T - \overline{H_S})}{2(1+f)a^2[(H_T - \overline{H_S}) + \overline{H_S}]} = F_{ST}$$

- Overdominance (no additivity), $\forall f$

  When $a = 0$, expression for V_B and V_{AW} become

$$V_B = d^2(1-f)^2 V(H_S)$$

and

$$V_{AW} = \frac{d^2(1-f)^2}{(1+f)}\left(\overline{H_S} - \frac{2}{n}\sum\left(H_{Si}\right)^2\right) = \frac{d^2(1-f)^2}{(1+f)}\left(\overline{H_S} - 2\overline{H_S}^2 - 2V(H_S)\right)$$

and Q_{ST} becomes:

$$Q_{STa\to 0} = \frac{(1+f)^2 V(H_S)}{((1+f)^2-4)V(H_S) + 2\overline{H_S}(1-2\overline{H_S})}$$

This is clearly very different from F_{ST} (equation 2)

- $f = 0$

  The expression for Q_{ST} does not simplify greatly when $f = 0$, as it remains a function of a, d, H_T, H_S and p:

$$Q_{STf\to 0} = \frac{2a^2(H_T - \overline{H_S}) - 4adCov(p, H_S) + d^2V(H_S)}{2a^2H_T - 4adCov(p, H_S) - 3d^2V(H_S) + 2d^2\overline{H_S}(1-2\overline{H_S})}$$

- $f = 1$

  When $f = 1$, since the dominance term d comes as a product with $(1-f)$ in V_B and V_{AW}, it disappears altogether from their expressions and therefore also from that of Q_{ST}, as expected. Thus, $Q_{STf\to 1} = F_{ST},\ \forall(a, d)$.

As we have seen, the expression for Q_{ST} in the presence of dominance and inbreeding is not simple. In order to gain a better understanding of its effect, we start with a two populations system and first show contour plots for F_{ST}, Q_{ST} and the difference $(Q_{ST} - F_{ST})$ for a trait encoded by one locus and two alleles as a function of the frequency of the recessive allele in two populations.

For a purely additive determinism, $F_{ST} = Q_{ST}$ and the difference $Q_{ST} - F_{ST}$ is therefore equal to zero for all points of the allele frequency space.

[Figure 1 about here.]

Figure 1 shows the contour plots for the case $a = 1, d = 1$ and $f = 0$. F_{ST} (represented in panel A) is null when the frequency is the same in the two populations, and increases as allele frequencies diverge between the two populations, to reach a maximum of one when one allele is fixed in the first population and the other allele is fixed in the second.

The contour plot for Q_{ST} is shown in panel B. When the allele frequencies are the same in the two populations, Q_{ST} is null, as expected. Difference in allele frequencies when the recessive allele is rare in the two populations brings less changes in Q_{ST} than F_{ST}. The effect of a difference in allele frequency increases as the recessive allele increases in frequency in both populations. When looking at the difference $Q_{ST} - F_{ST}$ (panel C) we observed that the difference is negative in the lower left part of the panel (when the recessive allele is rare in both populations), while it is positive on the upper right part (when the recessive allele is frequent). The negative area is larger than the positive one, and this is confirmed by integrating over the surface of allele frequencies: averaged over the allele frequency space, $Q_{ST} = 0.162$ while $F_{ST} = 0.186$. Thus, the expected difference between Q_{ST} and F_{ST} when there is dominance is negative.

[Figure 2 about here.]

Figure 2 shows a contour plot of the difference between Q_{ST} and F_{ST} for different levels of dominance and inbreeding. Panel A and B represents the case $a = 1, d = 1$ seen in Figure 1. $f = 0$ for panel A and this is therefore the same as panel C of Figure 1. In panel B, $f = 0.8$, and we see that the difference between Q_{ST} and F_{ST}vanishes. It is ten-fold lower than with no inbreeding. And the mean value for Q_{ST} is now 0.185, very close to the average $F_{ST}(= 0.186)$.

Panel C and D of figure 2 represent the case of strict overdominance ($a = 0; d = 1$). With strict overdominance and $f = 0$, a large area covering the secondary diagonal is negative (panel C), and a much smaller portion of the contour plot has positive values for the difference. When integrating over the surface, the average Q_{ST} is 0.09. Therefore, with strict overdominance, Q_{ST} is on average much lower than F_{ST}. With $f = 0.8$ (panel D), the area where the difference between Q_{ST} and F_{ST} is negative reduces drastically while that where it is positive increases. And indeed, average Q_{ST} when $f = 0.8$ is 0.186, as is average F_{ST}. High inbreeding therefore cancels out the effect of overdominance on Q_{ST}.

Computer simulations With many loci and alleles, analytical results become intractable when there is dominance and inbreeding. We therefore used computer simulations to generate data under different levels of population structure, inbreeding and trait determinism. Two types of simulations were used, one based on allele frequencies and the other on individuals.

Allelic frequencies

- First we drew allelic frequencies from Dirichlet distributions (Kingman 1977). Overall allelic frequencies $[p]$ is a vector with its element obtained from a Dirichlet distribution of parameter 1, equivalent to a uniform distribution. To obtain frequencies at each locus in the different populations, a Dirichlet distribution with parameter $2Nm[p]$, where Nm is the number of migrants between population, was used (Beaumont 2005).

- From these allele frequencies, F_{ST} was obtained classically as $1 - \frac{\overline{H_S}}{H_T}$, where $\overline{H_S} = \frac{\sum_{i=1}^{n}(1-\sum_{j=1}^{nl}\sum_{k=1}^{nk} p_{ijk}^2)}{n}$. Similarly, H_T was estimated as $1 - \sum_{j=1}^{nl}\sum_{k=1}^{nk} p_{jk}^2$, where p_{jk} is the realized overall allele frequency $p_{jk} = \frac{\sum_{i=1}^{n} p_{ijk}}{n}$ (i.e., it is not the original theoretical frequency $[p]$ from the Dirichlet distribution). To account for bias due to the number of samples, $H_T{}' = \frac{n}{n-1}(H_T - \overline{H_S}) + \overline{H_S}$ (Nei 1987) was used instead of H_T in the expression of F_{ST}.

- Traits were encoded by ten ten-allelic loci. Trait values were simulated by assigning to each allele at each locus an additive value drawn from a normal distribution. Similarly, to obtained dominance effect of each genotype, a value drawn from a normal distribution was assigned to the dominance deviation of the genotype. The sum of the two additive effects and the dominance deviation gives the genotypic value of this genotype at the locus considered. Genotypic values for multi-locus genotypes are obtained by summing the contributions of the individual loci, since we assume no epistasis. We also used exponential distributions instead of normal to draw additive value and dominance deviations, but this did not alter the results.

- Once all these values are assigned, the within population additive variance is estimated as $V_{Aw} = 2\sum_{j=1}^{nl}\sum_{i=1}^{nk} p_{ij}e_{ij}\alpha_{ij}$ (Lynch and Walsh 1998), with expressions for e_{ij} and α_{ij} given above (equation 4); and the among population variance of trait mean is simply that. Q_{ST} estimated this way is denoted ${Q_{ST}}^p$ where p stands for parent. Note that ${Q_{ST}}^p$ cannot be estimated in experimental situations, as one would need allelic frequencies for all alleles contributing to the trait and the genotypic values for all genotypes.

[Figure 3 about here.]

Figure 3 shows the relation between F_{ST} and ${Q_{ST}}^p$ for pure additivity (panels A and B), dominance (panels C and D) and super dominance (panel E and F) under no inbreeding (panels A, C and E) or strong inbreeding ($f = 0.8$, panels B, D and F).

Under strict additivity, ${Q_{ST}}^p = F_{ST}$, as expected, and independently of the inbreeding coefficient. For traits with dominance and under random mating (Figure 3 panel C), Q_{ST} becomes lower than F_{ST} on average, and this tendency increases as populations get more structured. But this effect disappears in inbred populations (Figure 3 panel D). With strict overdominance and under random mating (panel E), the pattern observed with dominance is enhanced, and ${Q_{ST}}^p$ is much lower than F_{ST}, the more so for very structured populations.

With selfing and strict overdominance (Figure 3 panel F), ${Q_{ST}}^p$ is larger than F_{ST} for weakly structured populations, and lower for those that are strongly structured.

The results presented in Figure 3 are for simulations with 10 populations. The effect of the number of populations involved is presented in Figure 4, where only the situation with purely additive traits under random mating is presented. This figure shows very clearly that with two populations (panel A), the variance among replicates is huge, still large with 5 populations (panel B), and much smaller with 50 populations (panel D).

[Figure 4 about here.]

Individual Based Model The results just presented are for a theoretical situation where both allele frequencies at all loci involved in the trait and genotypic values for all genotypes are known, but this is never the case. When experimentalists estimate Q_{ST}, they use covariance among relatives to estimate additive variance rather than the allele frequencies at the loci underlying the trait, since these loci are generally unknown. In order to mimic this real situation we used an Individual Based Model with the following features:

- We used EASYPOP (BALLOUX 2001) to generate genotypes from an individual based finite island model, where islands exchange migrants at a fixed rate m, constant among populations and across generations. For all the simulations, population size N was fixed at 50 hermaphroditic individuals, the number of populations n was also fixed at 50. For each individual, 100 loci with 20 allelic states each were simulated. The mutation rate was fixed at 0.001 and followed a KAM. Simulations were ran for 500 generations, at which point F_{ST} had reached its equilibrium value for all levels of migrations. These were fixed at $0.002, 0.005, 0.01, 0.02, 0.05, 0.1$ and 0.2, corresponding to Nm values of $0.1, 0.25, 0.5, 1, 2.5, 5$ and 10 respectively. Two selfing rates were used, either 0 or 0.8. Genotypes of the last generation were stored for further processing.

- Traits were encoded as in the simulations on allelic frequencies, by assigning additive

values drawn from a normal distribution to each allele at each locus and dominance deviation to each genotype.

- To estimate F_{ST} we used the genotypes at the trait loci of the parents, and calculated F_{ST} using the method of Weir and Cockerham (1984) implemented in Fstat (Goudet 1995). To estimate ${Q_{ST}}^o$ (where o stands for offspring), we proceeded as follows: a number of parents were chosen from each population of the island model. From these parents, a number of half-sib families (one male mated to ten different females) was established, with 10 offspring each (one offspring per female). We used either the full data set (10 individuals from 50 families from 50 populations, a total of 25000 individuals) or subsamples of 1000 offsprings from each data set, using different sampling scenarios presented in table 2.

[Table 2 about here.]

These experimental sampling designs are similar to those used in several studies estimating ${Q_{ST}}^o$, with total number of individuals in the 1000 (e.g. Lynch *et al.* 1999, Morgan *et al.* 2005, Palo *et al.* 2003, Spitze 1993). Often however, the total number of individuals used to infer Q_{ST} is less than 1000 (e.g. Bonnin *et al.* 1996, Petit *et al.* 2001, Steinger *et al.* 2002).

- A classical nested ANOVA was used to estimate the different variance components. V_{AW} is estimated as four time the among family component of variance V_{fam}, while V_B is simply the among population variance component.

Figure 5 shows the relation between F_{ST} and ${Q_{ST}}^o$ for additive (panels A and B), dominant (panels C and D) and superdominant (panels E and F) traits, for random mating (panels A, C and E) and selfing (panel B, D and F). For all panels of Figure 5, estimation of ${Q_{ST}}^o$ is based on 50 families of 10 half-sibs from 50 populations. Under strict additivity

(panel A and B), ${Q_{ST}}^o = F_{ST}$, and there is no difference between random mating and selfing populations. The observed pattern is congruent with that obtained for ${Q_{ST}}^p$ (Figure 3, panels A and B).

For traits with dominance (Figure 5, panels C and D), ${Q_{ST}}^o \leq F_{ST}$, and the difference increases as population structure increases. This is observed both for random mating and selfing populations, and there seems to be very little differences in ${Q_{ST}}^o$ between the two mating systems.

Last, panels E and F of Figure 5 show the effect of overdominance. Here, the pattern observed with dominance (a lower ${Q_{ST}}^o$ than F_{ST}, and the difference increasing with population structure) is amplified.

[Figure 5 about here.]

Effect of the crossing design. We have seen that with allele frequency based estimates of Q_{ST}, the effect of dominance on ${Q_{ST}}^p$ disappears as selfing increases (Figure 3 panel D), but when Q_{ST} is estimated with a half-sib design, the pattern ${Q_{ST}}^o < F_{ST}$ remains (Figure 5 panel D). However, the half-sib design is likely to unduly inflate additive variance estimates for a species that commonly self, and for strongly selfing species, experimentalists often use selfed progeny to estimate the different genetic variance components and hence Q_{ST} (e.g. Bonnin *et al.* 1996; Steinger *et al.* 2002). With a selfed progeny design, additive variance cannot be singled out from dominance variance, but for a high selfer, dominance variance is not naturally expressed as homozygous genotypes are transmitted intact to the next generation. With selfed progeny, Q_{ST} is estimated as $\frac{\sigma^2_B}{\sigma^2_B+\sigma^2_{Fam}}$, which amounts to assume complete selfing (see equation 1).

Using individual based simulations with high selfing rate ($s = 0.889$ $f = 0.8$), we compared estimates of Q_{ST} obtained from either half sibs or selfed progenies. Figure 6 shows the results. Panels on the left of Figure 6 were obtained using a classical half-sib design, while those on the right were obtained using a selfing design. With pure additivity (panel

A and B), the two crossing designs give equivalent results. With dominance, estimates of Q_{ST} obtained from a selfed design (panel D), are slightly lower than, but closer to F_{ST} than those obtained from a half-sib design (panel C). This is particularly true for populations that are strongly structured. Hence, when the species under scrutiny is mainly selfing, estimates of Q_{ST} obtained from selfed progeny are less influenced by dominance, thus preferable, to estimates obtained from a half-sib design. Another advantage of the selfing design is that it does not require a precise assessment of the inbreeding coefficient of the population (a pre-requisite for the half-sib design).

Last, panels E and F of Figure 6 show the effect of the crossing design on traits that are purely overdominant. Panel E shows that under strict overdominance, Q_{ST} is even lower than under dominance when Q_{ST} is estimated from a half-sib design in a species with high selfing. If selfed progeny are used instead of half-sib, Q_{ST} does not differ from zero whatever the level of population structure. This is expected, as under overdominance, homozygote genotypes all have the same trait value. Selfed progeny from highly selfed parent are strongly homozygous in all populations, and therefore traits means is also identical among populations. Note that this is an artefact of having strict overdominance (i.e, the complete absence of additive effects).

[Figure 6 about here.]

Sampling strategies. The effect of different sampling strategies on estimation of ${Q_{ST}}^o$ is shown on Figure 7. The box-plot representation gives a fair idea of the distribution of ${Q_{ST}}^o$ under these four sampling strategies. The worst scenario is strategy A (50 families of 10 individuals in 2 populations), which shows the largest variance for all levels of population differentiation and a negative bias that increases in magnitude as differentiation increases.

Strategies C (20 populations) and D (40 populations) are best overall, with strategies C being slightly better for low structure and strategies D better for high structure. For scenarios C and D, the interquartile range is very similar to that under exhaustive sampling

(labelled T on Figure 7).

[Figure 7 about here.]

DISCUSSION

While dominance can theoretically either increase or decrease Q_{ST} relative to its expectation under strict additivity, we have shown that, on average, dominance decreases the value of Q_{ST}, and the more differentiated the populations, the stronger the effect. Thus, we conclude that dominance is unlikely to cause the pattern $Q_{ST} > F_{ST}$. Since this pattern was also shown to be unlikely under epistasis (Whitlock 1999, Lopez-Fanjul *et al.* 2003), we argue that when Q_{ST} is larger that F_{ST}, it is a good indicator of the presence of directional selection for different local optima. $Q_{ST} < F_{ST}$, on the other hand, could be the result of several factors other than homogenizing selection.

These results contrast with those obtained by Lopez-Fanjul *et al.* (2003), who found that the effect of dominance would more often increase Q_{ST} relative to F_{ST} than the reverse. There may be several reasons for this. First, Lopez-Fanjul *et al.* (2003) focused on populations that just underwent a severe bottleneck, and bottlenecks are known to alter (increase or decrease) the genetic variance both within and between lines (Robertson 1952, Willis and Orr 1993, Cheverud and Routman 1996, Naciri-Graven and Goudet 2003, Barton and Turelli 2004). Second, to compare F_{ST} and Q_{ST}, they did not use the allele frequencies at the loci coding for the trait as we did here, but used the expectation of the inbreeding coefficient among recently bottlenecked populations. Third, they looked at the effect of a one generation bottleneck of 2 individuals, which would correspond to an F_{ST} of 0.25 on average and did not investigate (as we did here) a range of population structure. Note that we also find situations in which $Q_{ST} > F_{ST}$, when the recessive allele is very common in most populations. But this situation is unlikely to be found frequently in nature, as recessive alleles are often deleterious, thus under the action of purifying selection, and therefore, at low frequencies (Naciri-Graven and Goudet 2003, Barton and Turelli

2004).

In general, empirical studies tend to find $Q_{ST} > F_{ST}$ (see reviews in Merila and Crnokrak (2001) and McKay and Latta (2002)). Can we conclude from this pattern that directional selection is in action? Our results show that non-additive gene actions are not the likely culprits, but other biases could produce this pattern:

- Hendry (2002) pointed out that mutation is also likely to alter the relation between Q_{ST} and F_{ST}. The deflating effect of large mutation rate on F_{ST} is well known (Hedrick 1999; Balloux *et al.* 2000). If Q_{ST} is less sensitive to mutation than F_{ST}, or if mutation rate at trait loci is lower than at marker loci, then the mutation rate in itself can create the pattern expected under the action of directional selection. On the other hand, the mutation rate on a quantitative trait coded by several loci might be larger than that of one molecular marker. Thus, we concur with Hendry (2002): the potential effect of mutation rate on the relation between F_{ST} and Q_{ST} deserves a thorough investigation.

- The large variance in Q_{ST} estimates based on few populations (and in many field situations, only a few populations are available) limits the statistical power of a test of the relation $F_{ST} = Q_{ST}$. O'Hara and Merila (2005) recently investigated the statistical properties of estimators of Q_{ST}, and came to the same conclusion: with less than a dozen populations, the variance in Q_{ST} is huge. We showed that this is particularly the case for very differentiated populations ($F_{ST} > 0.2$). With less differentiation, the problem seems less acute. We also showed that with few populations, estimates of Q_{ST} seem to be biased downward. Thus, the pattern $Q_{ST} > F_{ST}$ is unlikely due to a statistical artifact. Note that these arguments are only verbal, and more work is clearly necessary to refine the statistical tools available. In particular, our investigation of the effects of the sampling strategies needs to be pursued: we modelled traits that are purely genetically determined, and the effect of environmental variance on the

precision of Q_{ST} estimates is not known, but is likely to inflate the variance of Q_{ST}.

- It would be interesting to investigate the behaviour of Q_{ST} under the joint action of selection and dominance. If the effect of dominance is just to hide recessive deleterious alleles, then recessive alleles will be rare and we saw that this is a situation where Q_{ST} is less than F_{ST}. Hence, the presence of deleterious recessive alleles should tend to make Q_{ST} even lower than F_{ST}. If both purifying selection and directional selection for different optima is occurring, the deflating effect of dominance on Q_{ST} might cancel out the enhancing effect of directional selection. Hence, the pattern $Q_{ST} = F_{ST}$ might reflect the joint action of these two selective forces rather than the absence of selection. A similar investigation on the effect of epistasis is also necessary.

CONCLUSIONS

Despite these caveats and shortcomings, we have clearly shown that the pattern $Q_{ST} > F_{ST}$ is unlikely for neutral traits with non-additive gene action. Importantly, we have also shown that estimates of Q_{ST} are only reliable if based on many sampled populations. Providing that this is the case, the comparison between Q_{ST} and F_{ST} will remain useful in documenting the presence (or not) of local adaptation.

ACKNOWLEDGMENTS

We thank Guillaume Evanno, Benoît Facon, Juha Merilä, Bob O'Hara and an anonymous reviewer for useful comments on previous versions of this manuscript. JG was supported by grant 31-108194/1 from the Swiss National Science Foundation.

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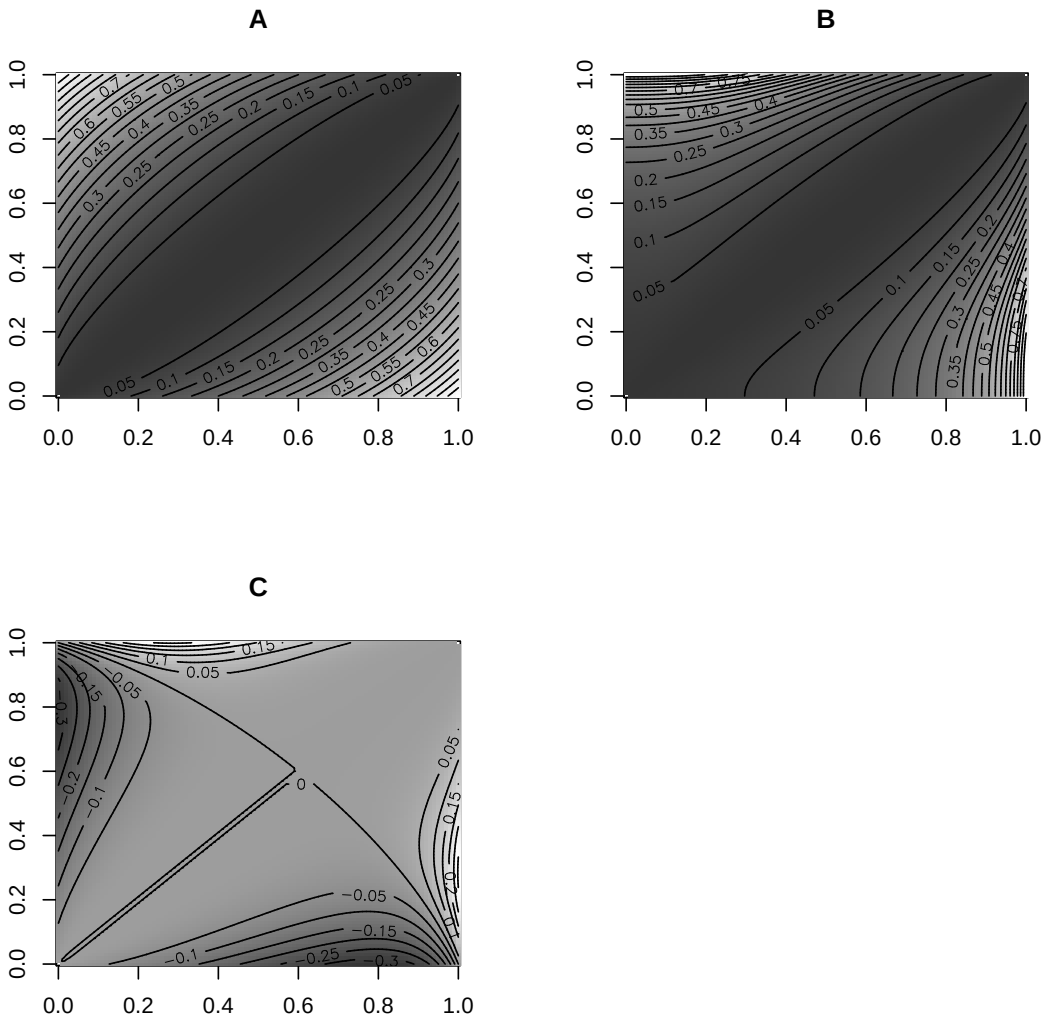

Figure 1: Contour plots of F_{ST} (panel A), Q_{ST} (panel B) and the difference $Q_{ST} - F_{ST}$ (panel C) for two populations, as a function of the recessive allele frequencies in population one (x-axis) and two (y-axis). The trait is dominant (additivity a and dominance d set to 1), and inbreeding is 0.

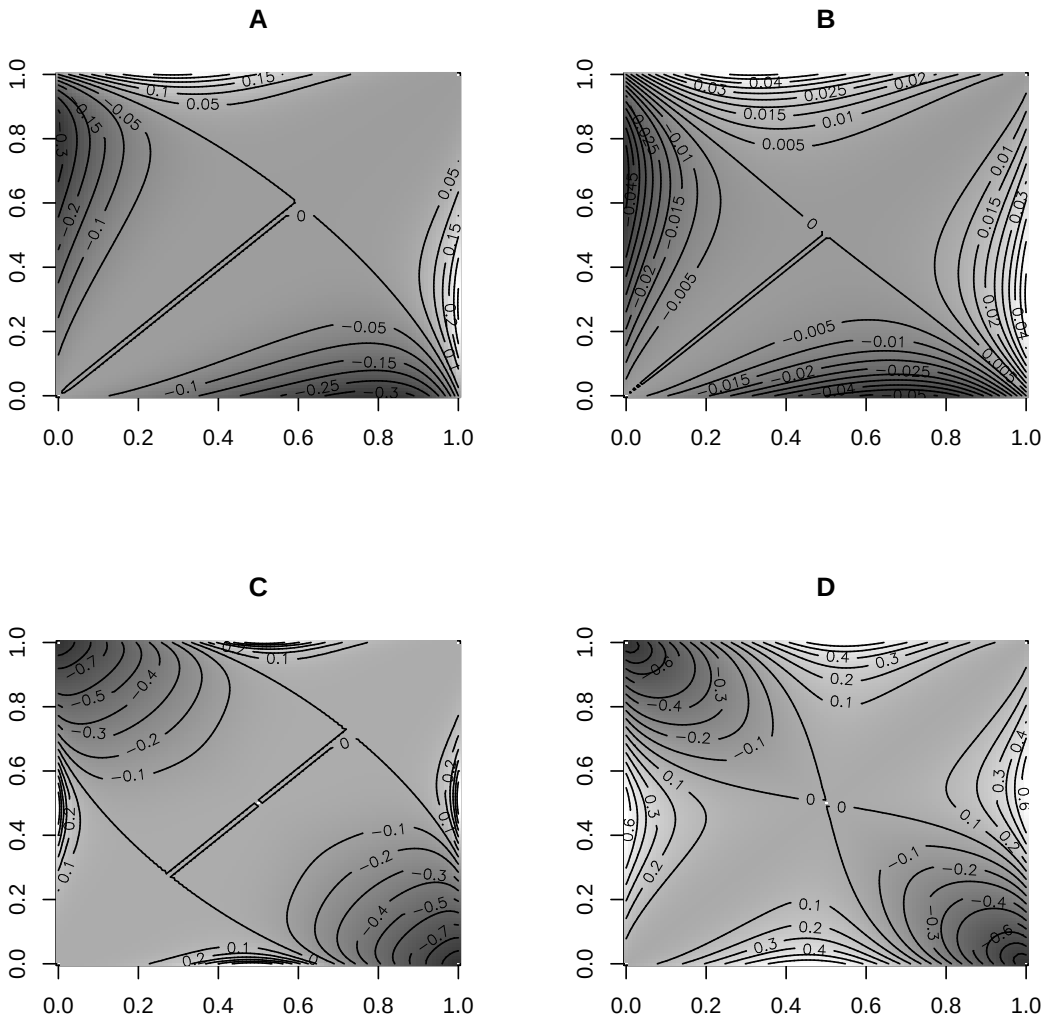

Figure 2: Contour plots of the difference $(Q_{ST} - F_{ST})$ for two populations and different levels of dominance and inbreeding, as a function of the recessive allele frequencies in population one (x-axis) and two (y-axis). Panels A and B are for $a = 1$, $d = 1$, with $f = 0$ in panel A and $f = 0.8$ in panel B. Panels C and D also show contour plots of $Q_{ST} - F_{ST}$ but for an overdominant situation ($a = 0$, $d = 1$). In panel C, $f = 0$ while $f = 0.8$ in panel D.

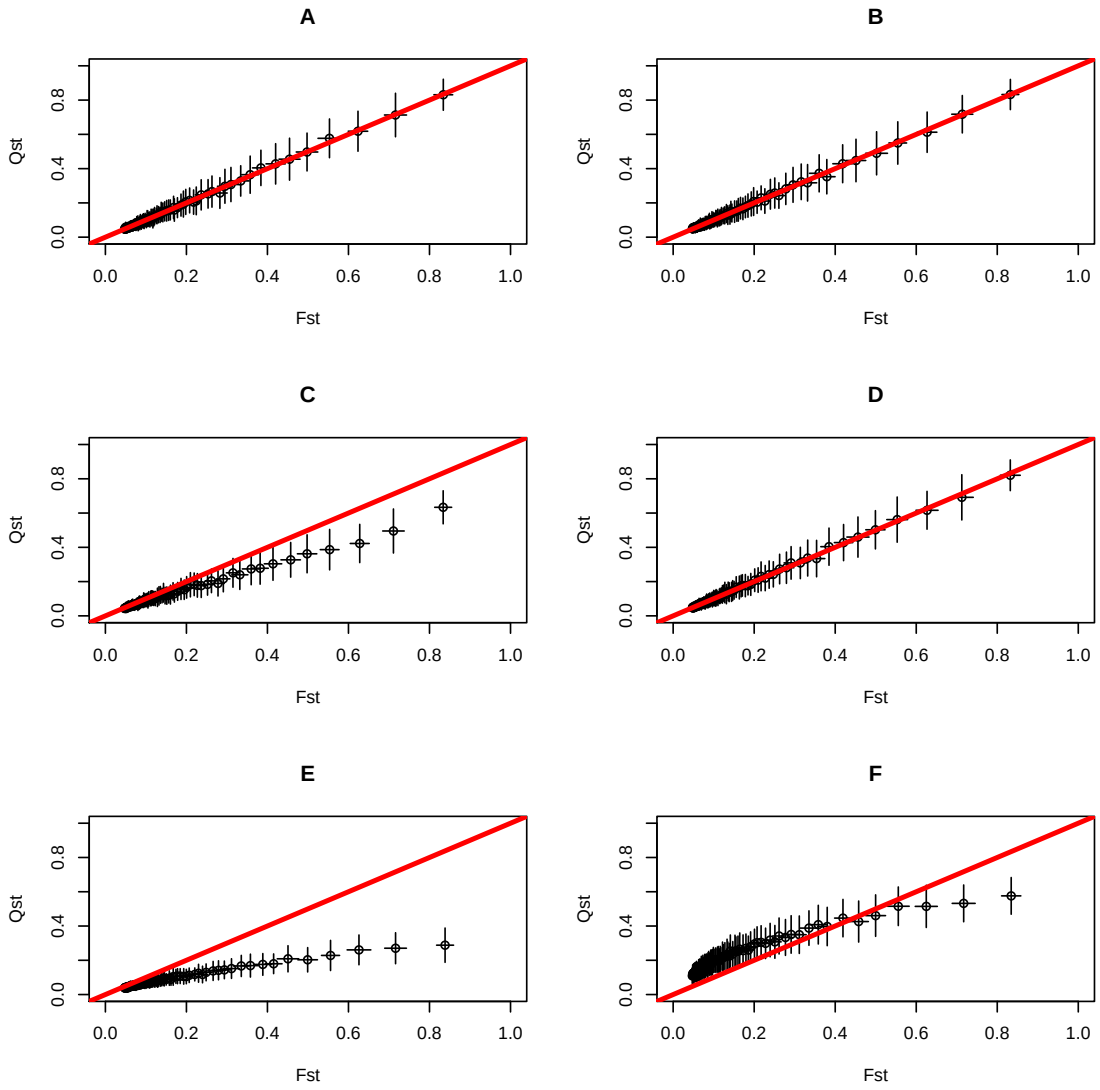

Figure 3: $Q_{ST}{}^{p}$ versus F_{ST} for a trait coded by 10 10-allelic loci. Additive effects and dominance deviation are drawn from a normal distribution. For all panels, $n = 10$. Panel A, C and E: $f = 0$; panel B, D and F $f = 0.8$. Panel A and B: purely additive trait; Panel C and D: dominant trait; panel E and F: overdominant trait. Means based on 100 replicates. F_{ST} and $Q_{ST}{}^{p}$ are calculated as ratio of sums rather than the sums of ratios. Error bars represents ± 1 standard deviation. The solid line is the line of equality between F_{ST} and $Q_{ST}{}^{p}$.

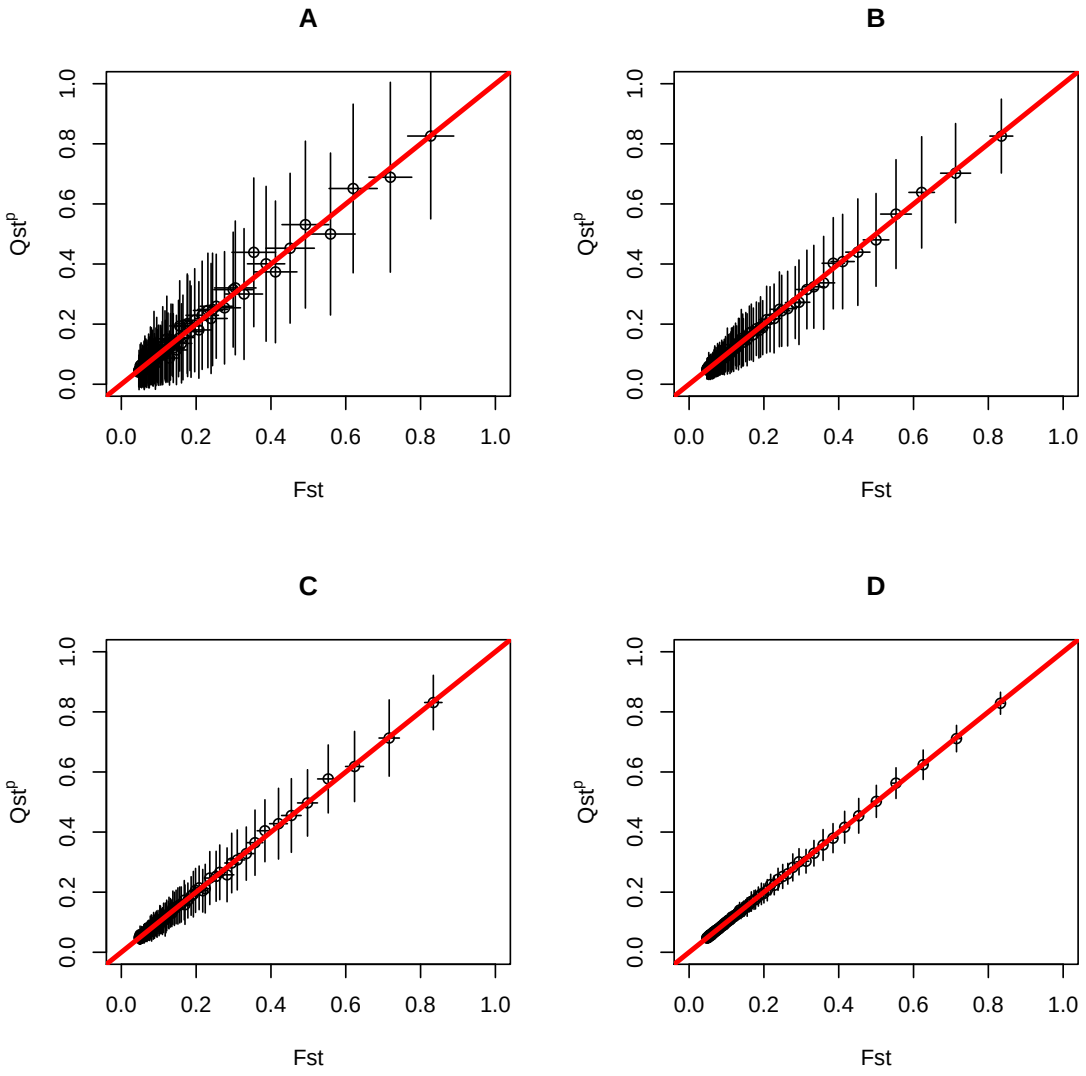

Figure 4: ${Q_{ST}}^p$ versus F_{ST} for a trait coded by 10 10-allelic loci. For all panels, purely additive traits and no inbreeding. Panel A: $n = 2$; panel B: $n = 5$; panel C: $n = 10$; panel D: $n = 50$. Means based on 100 replicates. F_{ST} and ${Q_{ST}}^p$ are calculated as ratio of sums rather than the sums of ratios. Error bars represents ± 1 standard deviation. The solid line is the line of equality between F_{ST} and ${Q_{ST}}^p$.

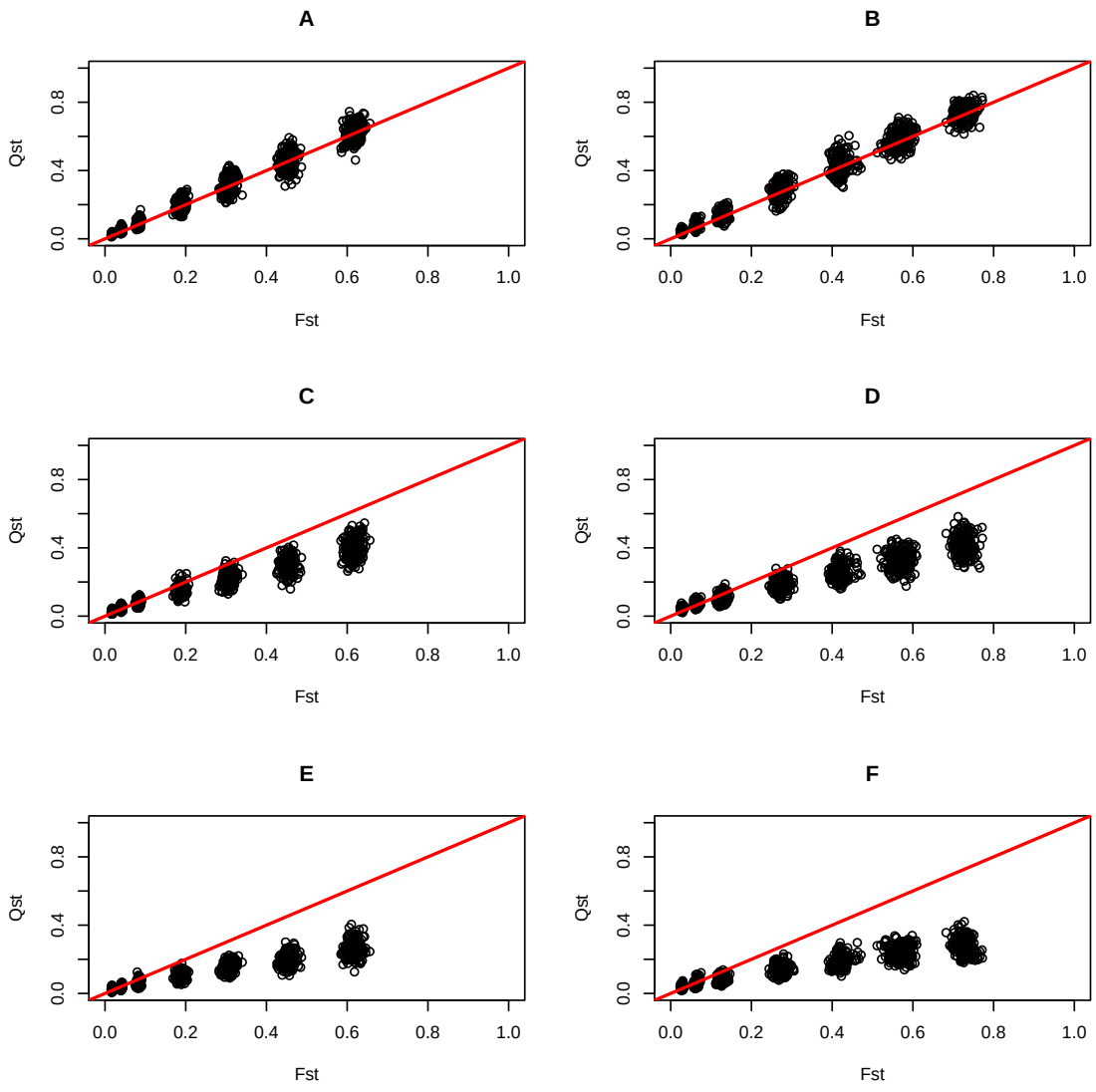

Figure 5: ${Q_{ST}}^o$ as a function of F_{ST} for different trait determinism and two levels of selfing. Estimation of ${Q_{ST}}^o$ based on 50 families of 10 half-sibs from 50 populations. Additive and dominance effect were drawn from a normal distribution. Panel A, C and E: random selfing. Panel B, D and F: s=0.8; panel A and B: additive traits; Panel C and D traits with both additivity and dominance. Panel E and F: overdominant traits

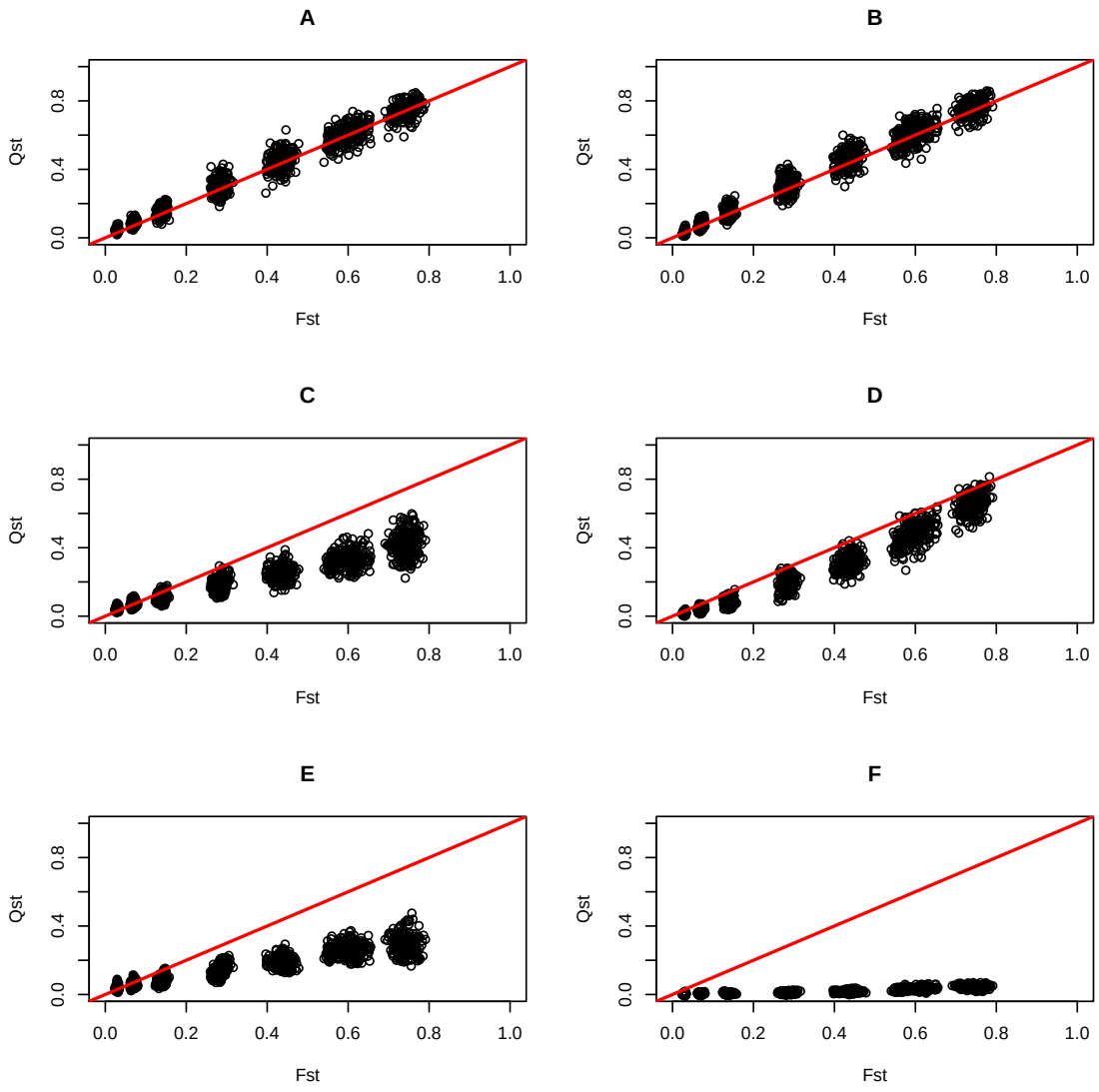

Figure 6: Effect of the crossing design used to infer Q_{ST}. For all panels, $s = 0.889$ ($f = 0.8$), and sampling is exhaustive. Panel A, C and E: variance components were estimated using a true half-sib design. For this design, Q_{ST} was estimated as $Q_{ST} = \frac{(1+f)\sigma_B^2}{(1+f)\sigma_B^2+8\sigma_{Fam}^2}$. Panel B, D and F: variance components were estimated using 10 selfed offspring for each individual. For this design, Q_{ST} was estimated as $Q_{ST} = \frac{\sigma_B^2}{\sigma_B^2+\sigma_{Fam}^2}$. Panel A and B: purely additive trait. Panel C and D: dominant trait. Panel E and F: overdominant trait (no additivity).

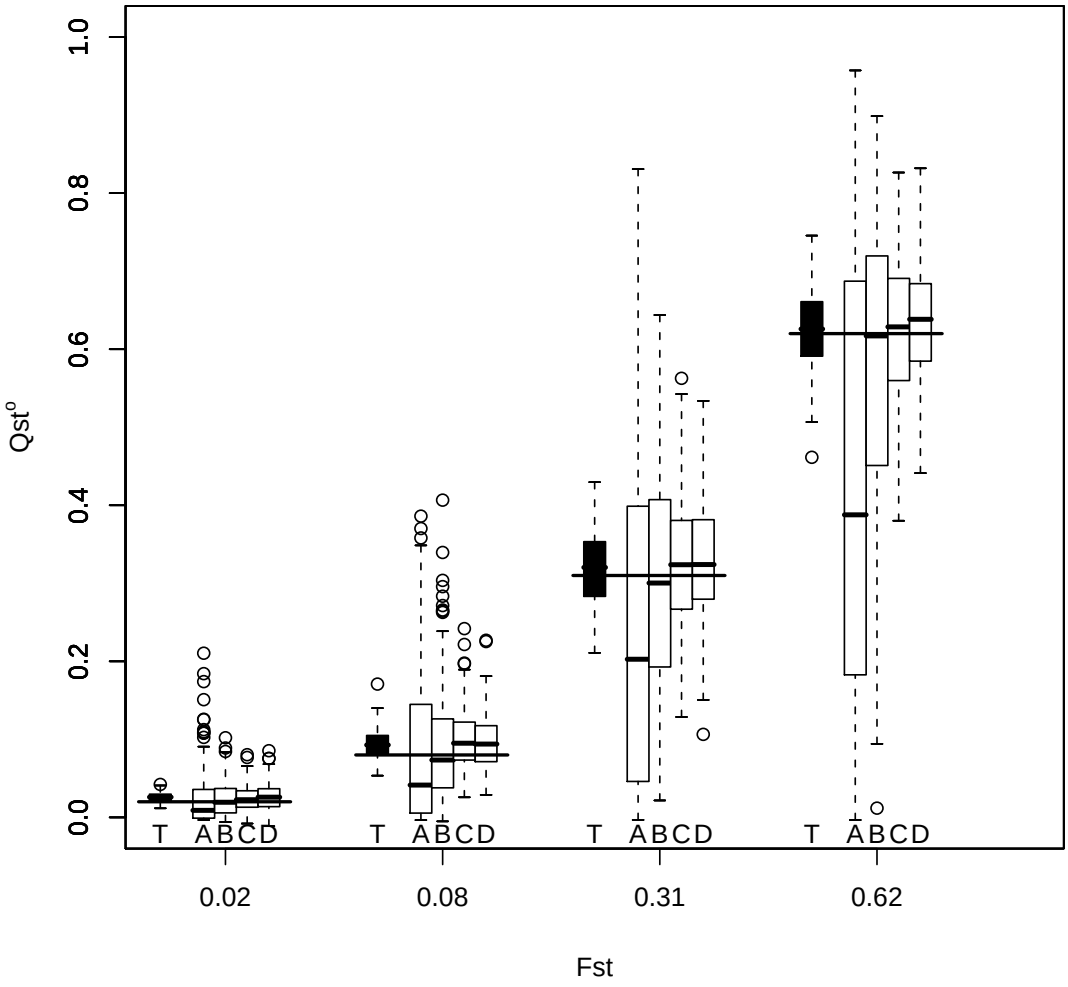

Figure 7: Effect of different sampling strategies on ${Q_{ST}}^o$ estimation for four different levels of population structure. The trait is purely additive and $s = 0$. For each of the four levels of population structure, leftmost box-plot (labelled T): exhaustive sampling (50 half-sib families of 10 individuals from 50 populations. The other four sampling schemes are based on a total of 1000 individuals. From left to right A: 50 families of 10 individuals from 2 populations; B: 20 families of 10 individuals from 5 populations; C: 10 families of 5 individuals from 20 populations; D: 5 families of 5 individuals from 40 populations. The long horizontal black segments are drawn at the expected value of F_{ST}. Boxes correspond to the interquartile range and the small horizontal black segments give the median of Q_{ST}

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Genotype	AA	AB	BB
Genotypic value	$-a$	d	a
Frequency in pop i	$p_i^2 + p_i q_i f$	$2p_i q_i(1-f)$	$q_i^2 + p_i q_i f$

Table 1: Genotypes, their genotypic values and frequencies in a population with inbreeding coefficient f due to regular inbreeding

Name	Populations	Families	Individuals
T	50	50	10
A	2	50	10
B	5	20	10
C	20	10	5
D	40	5	5

Table 2: Sampling designs used to infer ${Q_{ST}}^o$. Sampling designs A-D consist of 1000 individuals in total