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Simple test statistics for major gene detection: a numerical comparison

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Summary. We compare 22 simple tests for the detection of major gene segregation in livestock populations. These tests belong to two groups: methods based on the comparison of within-family distribution and methods based on the comparison of parents' and offspring performances. The power of the 22 tests and the robustness of the two more powerful of these 22 are evaluated by simulation. Thirteen types of major loci, differing in the within-genotype means, variances or alleles frequencies, are studied. Thirty hierarchically balanced populations defined by the number of sire families (5–20), dams per sire (1–20) and progenies per dam (1–20) are simulated. The quantiles are estimated from 2000 samples, the power from 1000 samples and the robustness from 100 samples. The more powerful tests are the within family-variance heterogenity test (Bartlett test) and the within-family mean-variance regression (Fain 1978). Their robustness may be very low, in particular when the trait distribution is skewed.

Key words: Major gene – Simulation

Introduction

Evidence from drosophila, mice and domestic animal species supports the hypothesis that quantitative traits are often under the influence of a number of genes, a few having substantial effects (Piper and Shrimpton 1989; Mayo et al. 1982). In recent years several genes having a major effect on commercial traits have been identified in livestock: the dwarf gene in poultry (Mérat and Ricard 1974), the halothane sensitivity gene (Ollivier 1980) and the *RN* gene (Le Roy et al. 1990) in pigs, the *Booroola* gene in sheep (Piper and Bindon 1982) and the milk flow gene in goats (Ricordeau et al. 1990). These discoveries, as well as the development of biotechnology, have increased the interest in statistical methods for the detection of such variability. Generally, the structure of the populations studied was not designed with a view to detecting major genes, thus the discovery of such a gene was most often a byproduct of other experiments.

Simple indicators of major gene segregation have been proposed in the past. More or less powerful, not very robust but very easy to calculate, they could be used in a systematic way when observing populations, either for selection purposes or for experimentation. In this paper we compare, by simulation, the power and robustness of some of these methods. Before describing the populations simulated, we give the rationale and formulae for each of the indicators.

Description of the compared methods

The general principle is that the trait distribution parameters change when a major gene is segregating, as compared to the strictly polygenic (or to the sporadic) situation. We shall call *H0* and *H1* the strictly polygenic and mixed (a major gene + polygenes) inheritance, respectively. The methods differ mainly in the way the genetic structure of the population is considered.

Methods based on the global distribution of the trait

With these methods no genealogical information is used. The rationale for their use is that when a major gene is segregating, the trait distribution in the observed population is a mixture of subdistributions. Depending on the

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differences between the means and on the proportions of the components of the mixture, the resulting global distribution may be multimodal or simply skewed. Thus, tests of normality, skewness and kurtosis have been suggested by Hammond and James (1970), Hanset and Michaux (1985a) and Spielman et al. (1978) as first major gene indicators. These tests are of very limited robustness.

Testing the global distribution as a mixture (see Titterington et al. 1985 for a review of the statistical problem) requires much more computing but adds little to the genetic interpretation of the results. MacClean et al. (1976), Morton et al. (1978), Spielman et al. (1978), Hanset and Michaux (1985a, b) and Hoeshele (1988) used this test, in a maximum likelihood context, as an indicator of major gene segregation. More recently, El Amraoui and Goffinet (1989) proposed a non-parametric approach.

Methods based on the comparison of within-family distributions

In this family of tests, the first genealogical information is considered through the distribution of the data in sib families. The rational for their use is that when a major gene is segregating, the within-family distribution of the trait depends on the parent genotype, inducing heterogeneity of these distributions (Tables 1 and 2).

Within-family variance heterogeneity. Mérat (1968), Fain (1978) and Hanset and Michaux (1985b) suggested the use of the Bartlett test (1937), which is a χ^2 test of within-group homogeneity variances. Let s_i^2, the estimation, with f_i degrees of freedom, of the i^{th} ($i=1, \ldots, a$) variance, σ_i^2. The Bartlett test statistic is the ratio $\frac{M}{C}$, where:

$$M = \left(\sum_i f_i\right) \log(s^2) - \sum_i f_i \log(s_i^2)$$

with:

$$s^2 = \sum_i f_i s_i^2 \Big/ \sum_i f_i$$

and

$$C = 1 + \frac{1}{3(a-1)} \left(\sum_i \frac{1}{f_i} - \frac{1}{\sum_i f_i} \right)$$

is distributed under *H0* ($\sigma_i^2 = \sigma^2 \, \forall i$, that is "no major gene") as a χ^2_{a-1}.

Table 1. Within full sib family distribution of a quantitative trait when a major gene is segregating with two alleles *A* and *a*. Hypotheses: Hardy-Weinberg equilibrium; within genotype variances equal

Parents' genotypes	Frequency[a] of the family	Mean[b]	Variance[c]	Potential number of modes
$AA \times AA$	p^4	μ_1	σ^2	1
$AA \times Aa$	$4p^3q$	$\frac{\mu_1+\mu_2}{2}$	$\sigma^2 + \left(\frac{\mu_1-\mu_2}{2}\right)^2$	2
$AA \times aa$	$2p^2q^2$	μ_2	σ^2	1
$Aa \times Aa$	$4p^2q^2$	$\frac{\mu_1+2\mu_2+\mu_3}{4}$	$\sigma^2 + \frac{3(\mu_1-\mu_3)^2+4(\mu_2-\mu_1)(\mu_2-\mu_3)}{16}$	3
$Aa \times aa$	$4pq^3$	$\frac{\mu_2+\mu_3}{2}$	$\sigma^2 + \left(\frac{\mu_3-\mu_2}{2}\right)^2$	2
$aa \times aa$	q^4	μ_3	σ^2	1

[a] $p=1-q$: allele *A* frequency
[b] μ_1, Mean value of the *AA* animals; μ_2, mean value of the *Aa* animals; μ_3, mean value of the *aa* animals
[c] $\sigma_1^2=\sigma_2^2=\sigma_3^2=\sigma^2$: within genotype variances

Table 2. Within half-sib family distribution of a quantitative trait when a major gene is segregating with two alleles *A* and *a*. Hypotheses: Hardy-Weinberg equilibrium; within genotype variances equal

Parents' genotypes	Frequency[a] of the family	Mean[b]	Variance[c]	Potential number of modes
AA	p^2	$p\mu_1+q\mu_2$	$\sigma^2 + pq(\mu_1-\mu_2)^2$	2
Aa	$2pq$	$\frac{p\mu_1+\mu_2+q\mu_3}{2}$	$\sigma^2 + \frac{p(\mu_1-\mu_2)^2+pq(\mu_1-\mu_3)^2+q(\mu_2-\mu_3)^2}{4}$	3
aa	q^2	$p\mu_2+q\mu_3$	$\sigma^2 + pq(\mu_2-\mu_3)^2$	2

[a] $p=1-q$: allele *A* frequency
[b] μ_1, Mean value of the *AA* animals; μ_2, mean value of the *Aa* animals; μ_3, mean value of the *aa* animals
[c] $\sigma_1^2=\sigma_2^2=\sigma_3^2=\sigma^2$: within genotype variances

Under *H1* ("mixed inheritance") the within-family variances σ_i^2 may take three (half-sib family) or four (full-sib family) values that depend on the parent's genotypes (Tables 1 and 2). In this case, the test statistic $\frac{M}{C}$ is distributed as a χ'^2_{a-1} where the non-central parameter depends on the true value of the σ_i^2.

A known defect of this test is its lack of robustness in the presence of non-normality of the distribution. Moreover, Mérat (1968) showed that the heterogeneity of variances is not all specific for a major gene segregation.

The power and robustness of this test have been studied by Fain (1978) and MacCluer and Kammerer (1984) for human type family distribution. We shall extend this study to livestock family structure considering two statistics, the first based on the within-sire family variance (*Barths*) and the second on the within-dam family variance (*Bartfs*).

Within family distribution heterogeneity. Mérat (1968) generalized the previous approach to the test of heterogeneity of skewness (g_1) and kurtosis (g_2) coefficients of the within-family distribution. The idea is that in families where a major gene is segregating (with at least one heterozygous *Aa* parent), g_2 will be negative. Because the asymptotic normality of g_2 requires a very large family size, Mérat (1968) suggested pooling the families into two groups (small and large within-family variance) and testing the negativity of g_2 for each of the two groups.

This test has been applied by Mérat (1971) and Hammond and James (1970), who obtained inconsistent results. We shall extend this study by considering the statistic $\frac{g_{2l}}{\sigma_{g_{2l}}} - \frac{g_{2h}}{\sigma_{g_{2h}}}$, g_{2l} and g_{2h} as being defined as the kurtosis coefficients of the families, the distribution variance of which are, respectively, below and above the mean variance, and $\sigma_{g_{2l}}$ and $\sigma_{g_{2h}}$ as their standard deviations. As in the Bartlett test, two statistics (*Meraths* and *Meratfs*) are studied, corresponding to the within-sire and within-dam definition of the family.

Within-family mean-variance regression. The families where the major gene is segregating (at least one *Aa* parent) have an intermediate mean and a large variance as compared with families of $AA \times AA$ or $aa \times aa$ parents, where the means are large (either positive or negative) and the variances small. Fain (1978) proposed the test of curvilinear relation between within family mean (μ_i) and variance (σ_i).

The corresponding model is

$$E(\log \sigma_i^2) = A + B_1 \mu_1 + B_2 \mu_i^2 + B_3 \mu_i^3$$

This test has been evaluated for human family structure by Fain and Ott (1976), Fain (1978), MacCluer and Kammerer (1978) and Mayo et al. (1980). It seems to be powerful but not robust to non-normality and heteroscedasticity.

We shall evaluate this test with a livestock family structure. The major gene hypothesis will be rejected when the *F* test of the model is not significant. As for the Bartlett and Mérat tests, the statistic will be defined for sire family (*Fainhs*) and dam family (*Fainfs*).

Methods based on the comparison of parents' and offspring performances

The underlying idea is that quite often when a major gene is segregating, a progeny appear more similar to one of its parents than to their mean value. Thus, the corresponding methods include the performance and genealogical structure of two (or three) generations.

Regression of the within-family variance over the mean of the parents. Studying double muscling in cattle, Hanset and Michaux (1985b) showed that when a major gene is present, the proportion of progeny showing a high phenotypic value is a discontinuous function of the sire (or dam) phenotype. They proposed testing the linearity of the regression of the proportion of double-muscled calves over the sire or dam phenotype.

Since this approach requires a more or less arbitrary definition of abnormality, we shall test the significance of the curvilinear regression between the logarithm of the full-sib family variance and the mean of the parents. The method will now be referred to *Hanfain*.

The Structured Exploratory Data Analysis (SEDA). Karlin et al. (1979), Carmelli et al. (1979) and Karlin et al. (1981) proposed three criteria for major gene detection:

1) The Major Gene Index (*MGI*), defined as:

$$MGI(\alpha) = \frac{E(|Z-(X+Y)/2|^\alpha)}{E(|Z-X|^{\alpha/2}|Z-Y|^{\alpha/2})}$$

where Z is the performance of a progeny, X of its sire, Y of its dam, and α a parameter to be tested (1/2, 1 or 2)

This index is estimated as:

$$MGI(\alpha) = \frac{\sum_{i=1}^{N} \frac{1}{K_i} \sum_{j=1}^{K_i} |Z_{ij}-(X_i+Y_i)/2|^\alpha}{\sum_{i=1}^{N} \frac{1}{K_i} \sum_{j=1}^{K_i} |Z_{ij}-X_i|^{\alpha/2}|Z_{ij}-Y_i|^{\alpha/2}}$$

K_i being the size of the i^{th} family ($i=1, \ldots, N$).

2) The Offspring Between Parents regression (*OBP*), defined as:

$$OBP(\beta) = \frac{1}{N} \sum_{i=1}^{N} \frac{1}{K_i} \sum_{j=1}^{K_i} \Phi(Z_{ij})$$

with:

$$\Phi(Z_{ij}) = \begin{cases} 1 & \text{if } 2\left|Z_{ij} - \dfrac{X_i + Y_i}{2}\right| \leq \beta |X_i - Y_i| \\ 0 & \text{elsewhere} \end{cases}$$

3) The Pairwise Midparental Correlation Coefficient (*MPCC*), defined as:

$$MPCC = \frac{\sum_{ij}(Z_{ij} - Z_{..})\left(\dfrac{X_i + Y_i}{2} - \dfrac{X_. + Y_.}{2}\right)}{\sqrt{\sum_{ij}(Z_{ij} - Z_{..})^2 \sum_i \left(\dfrac{X_i + Y_i}{2} - \dfrac{X_. + Y_.}{2}\right)^2}}$$

where $Z_{..}$, $X_.$ and $Y_.$ are the mean performances of progenies, sires and dams, respectively.

As above, the rationale for these criteria is that compared to the value corresponding to the polygenic situation, the quantity $Z - \dfrac{X+Y}{2}$ is higher than either $Z - X$ or $Z - Y$ when a major gene is segregating. Thus, *MGI* will be higher and *OBP* and *MPCC* lower for this type of inheritance.

From asymptotic considerations about the mean of the criteria under different transmission hypotheses, Karlin et al. (1981) gave rules for the interpretation of their value. For instance, an *MGI* below 1 should indicate polygenic transmission, near 1 a sporadic situation and above 1 monogenic inheritance.

A number of publications (Karlin et al. 1981; Karlin and Williams 1981; Mayo et al. 1983; Kammerer et al. 1984; Morton et al. 1982; Young et al. 1981) have evaluated the efficiency of *SEDA* either through simulations or on real data. All the populations studied were human populations.

A difficulty in the Karlin proposition is that the thresholds for the biological interpretation have no statistical meaning. Used as suggested, their criteria cannot be considered as test statistics since no error control is guaranteed. Instead of applying their propositions, we shall study the *MGI* and the *MPCC* as real test statistics, rejecting the major gene hypothesis (*H0*) when the value taken by the criterion is outside a 95% confidence domain, the corresponding threshold being calculated by simulation under *H0*.

For practically purposes we shall study *MPCC*, *MGI2* (α), as defined above, and *MGI3* (α), an extension proposed by Karlin et al. (1979), when three generations are considered:

$$\frac{E(|Z - (X+Y)/2|^{\alpha} |X - (P_X + M_X)/2|^{\alpha} |Y - (P_Y + M_Y)/2|^{\alpha})}{E(|Z-X|^{\alpha/2}|Z-Y|^{\alpha/2}) E(|X-P_X|^{\alpha/2}|X-M_X|^{\alpha/2}) E(|Y-P_Y|^{\alpha/2}|Y-M_Y|^{\alpha/2})}$$

where Z is the value of the progeny, X of its father, Y of its mother, P_X and M_X of its paternal grandparents and P_Y and M_Y of its maternal grandparents.

MGI generalized: the Famula test. Famula (1986) extended the *MGI* test, replacing the phenotypes X, Y and Z by "animal model" estimations of the genetic values u_X, u_Y and u_Z. He justified this generalization with three reasons: (1) the possibility of calculating *MGI* even for traits that are not measured on one or both parents (milk production, carcass measurements); (2) the opportunity of correcting the phenotype for different effects such as year or herd; (3) an expected better precision of the measurement ($var(\hat{u}) \leq var(y)$). This extension of the *MGI* test has been used recently by Woolaston et al. (1990) in an analysis for a major gene affecting parasite resistance in sheep.

We shall study the Famula test in a way similar to that for the *MGI*. Four values of α will be tested. The criterion will be referred to as *Famula* (α).

We shall also study two types of statistics which are simpler than the Famula criterion (which is based on the animal model) but which still consider its main features, i.e. the possibility of using *MGI* even for an individual that is not measured. Two situations will be considered for each of the two types of statistics: a sex-limited trait (the sire not being measured) and a trait measured after slaughter (both parents are not measured).

We consider hierarchical and balanced populations of n sire families with m dams/sire and d progenies/dam. Let y_{ij} be the measurement on the ij^{th} dam, z_{ijk} on the $ij\,k^{\text{th}}$ progeny, $z_{ij.}$ the mean of the ij^{th} dam's progeny, $z_{i..}$ of the i^{th} sire's progeny. The within-genotype heritability is denoted by h^2.

The first test statistic is based on the classical genetic evaluation methods.

(1) for the sex-limited traits (*Famul1*):

$$X = m d \frac{h^2}{2} z_{i..} \Big/ \left(1 + d(m-1)\frac{h^2}{4} + (d-1)\frac{h^2}{2}\right)$$

for the sires

$Y = h^2 y_{ij}$ for the dams

$Z = h^2 z_{ijk}$ for the progenies

(2) and for the progeny-limited traits (*Famul2*):

$$X = m d \frac{h^2}{2} z_{i..} \Big/ \left(1 + d(m-1)\frac{h^2}{4} + (d-1)\frac{h^2}{2}\right)$$

for the sires

$$Y = d \frac{h^2}{2} z_{ij.} \Big/ \left(1 + (d-1)\frac{h^2}{2}\right)$$ for the dams

$Z = h^2 z_{ijk}$ for the progenies.

The second statistic is simply based on the means, without any regression:

(1) for the sex-limited traits (*Famul3*):
$X = z_{i..}$ for the sires
$Y = y_{ij}$ for the dams
$Z = z_{ijk}$ for the progenies.
(2) and for the progeny-limited traits (*Famul4*):
$X = z_{i..}$ for the sires
$Y = z_{ij.}$ for the dams
$Z = z_{ijk}$ for the progenies.

Methods

The power and robustness of the indicators described have been evaluated through simulations for different population structures and modes of inheritance.

Principle of the methods

Let *H0* be the hypothesis of polygenic inheritance and *H1* that of mixed (polygenic + major gene) inheritance. Under *H0* we consider a trait distributed as normal (0, 1) with a heritability of 0.2.

For each of the test statistics and population structures studied, the rejection threshold at an $\alpha = 5\%$ level of *H0* is estimated from 2000 samples using the Harrel and Davis (1982) method.

Given these rejection thresholds, the power of the test statistic is estimated, for a variety of major gene characteristics, simulating 1000 samples in each case. The robustness of the more powerful of the studied statistics is evaluated in a similar way, but on a very limited sample size (100 replications/type of distribution).

Evaluation of the power: populations structures and type of gene

We consider hierarchical and balanced populations of n sire families with m dams/sire and d progenies/dam. Thirty population types are considered with $n = 5$, 10, 20 progenies/sire and different types of sire families:

(1) full sib: $(m = 1; d = 5, 10, 20)$
(2) half sib: $(m = 5, 10, 20; d = 1)$
(3) mixed: $(m = 2, d = 5; m = 5, d = 2; m = 4, d = 5; m = 5, d = 4)$

Some tests are based on the performances of three generations. We will consider in this case that the sires and dams (2^{nd} generation) are unrelated, i.e. that each of the grandparents has only one progeny.

Thirteen mixed inheritances are simulated (Table 3). In all cases a within major locus genotype heritability of 0.2 is assumed. The 13 modes of inheritance differ by the allele A frequency in the sire (p) or dam (q) population and by the within-genotype means μ_t and variances σ_t^2, where t is the indice (1, 2, 3) for AA, Aa, and aa genotypes. Table 4 gives a summary of the comparisons made among modes of inheritance.

Evaluation of the robustness

We shall see that from the different test statistics studied, the within-family variance heterogeneity (*Bartlett*) and the mean-variance regression (*Fain*) are most often the more powerful tests. Moreover, the distributions of the corresponding test statistics under *H0* are known: χ^2 for *Bartlett*, Fisher for *Fain*. The *H0* rejection thresholds are thus given without any simulation, which makes these statistics much more useful.

Table 3. Situations of mixed inheritance simulated for the evaluation of the tests power

Situation	Means			Standard deviations			Frequencies[a]		Polygenic heritability h^2
	μ_1	μ_2	μ_3	σ_1	σ_2	σ_3	p_m	p_f	
1	0	0	1	1	1	1	0.7	0.7	0.2
2	0	0	2	1	1	1	0.7	0.7	0.2
3	0	0	3	1	1	1	0.7	0.7	0.2
4	0	1	2	1	1	1	0.7	0.7	0.2
5	0	0	2	1	1	2	0.7	0.7	0.2
6	0	0	2	1	1	1	0.5	0.5	0.2
7	0	1	2	1	1	1	0.5	0.5	0.2
8	0	0	2	1	1	2	0.5	0.5	0.2
9	0	0	2	1	1	1	0.9	0.9	0.2
10	0	0	2	1	1	1	0.7	0	0.2
11	0	1	2	1	1	1	0.7	0	0.2
12	0	0	2	1	1	2	0.7	0	0.2
12	0	0	2	1	1	1	0.9	0	0.2

μ_1, σ_1, Mean value and standard deviation within genotype AA;
μ_2, σ_2, mean value and standard deviation within genotype Aa;
μ_3, σ_3, mean value and standard deviation within genotype aa
[a] p_m, Allele A frequency for the males; p_f, allele A frequency for the females

Table 4. Effect of the type of major locus on the tests power. Comparison of the different situations studied

Studied effect	Situations compared	Description
Deviation between the mean effects of the genotypes	1–2–3	–
	2–4	–
Dominance	6–7	Equal allele frequencies
	10–11	Homozygous *aa* dams
Deviation between the variances within-genotype	2–5	–
	6–8	Equal allele frequencies
	10–12	Homozygous *aa* dams
	2–6–9	–
Allele frequencies	4–7	Additivity
	5–8	Unequal within genotype variances
	10–13	Homozygous *aa* dams
	2–10	–
Dam population homozygous *aa*	4–11	Additivity
	5–12	Unequal within genotype variances
	9–13	Rare *a* allele

Nevertheless, these distributions are only asymptotic. The robustness of these methods (using the asymptotic thresholds) when the population size is limited has been evaluated. We consider 10, 20, 30, 40, 50 and 100 sire familes and, in each case, four values for the ratio *dams per sire / progenies per dam* of 20/1, 5/4, 4/5, and 1/20.

The robustness against a lack of normality has also been studied for the 50 sires family populations. Three types of non-normality are considered:

(1) Discrete distribution, with three categories. The data are generated assuming an underlying normal distribution for the genetic and environmental values. The observed phenotypes (x) are generated comparing the underlying phenotype y to thresholds (λ_i):
$x = 1$ if $y \leq \lambda_1$
$x = 2$ if $y \in]\lambda_1, \lambda_2] \ldots$
Three types of discrete distributions are considered, corresponding to the *Mérinos d'Arles* sheep (D11), *Lacaune* sheep (D12) and *Romanov* sheep (D13) litter size distribution as given by Bodin and Elsen (1989).

(2) Bimodal distribution (D2), the source of bimodality being independent of the family structure. The distribution is generated by adding randomly $+1$ or -1 (with probability 1/2) to the phenotypes simulated.

(3) Asymmetric distribution. Three types of asymmetric distributions are obtained from the normal y distribution. Using the Demenais et al. (1986) transformation the observed phenotype x is given by
$$x = \exp\left(\frac{1}{c}\ln(y\,c+1)\right) - 1$$
The parameter c (D31: c = 0.1; D32: $c = 0.3$; D33: $c = 0.5$) controls the asymmetry of the resulting distribution.

Results

Power

For each of the test statistics studied, the best results for a 5% level are given in Tables 5–9. Tables 5, 6 and 7 show the maximum power of the tests given by numbers of sires (n), dams per sire (m) for full-sib families and progeny per dam (d) for half-sib families. Table 8 gives the family structure effect when the population is made up of 20 sire families with 20 progeny. These four tables show the higher power of each test for the 13 modes of inheritance. In Table 9 the results are detailed according to the mode of inheritance (maximum power for the 30 family structures studied).

The power is always more than 50% for the Bartlett and Fain tests. The statistics *MPCC*, *Famul2*, and *Famul4* reach this value with 20 sires. The power of the other criteria is never higher than 50%.

All the statistics appear to be sensitive to sample size. From the tests showing a power less than 20% for a limited number of sires (Table 5), some have more than a two-fold increase of their power when n increases from 5 to 20 ($\times 6.5$ for *Fainhs*, $\times 2.8$ for *Hanfain* and $\times 2.6$ for *MPCC*), some are insensitive to the number of sires (*MGI2* (α), *Famul2*) and others have a power increasing by 50% or 100%. The tests which are powerful for a limited number ($n = 5$) of sires reach a 100% power when $n = 20$ (*Bartfs*, *Barths* and *Fainfs*). The Bartlett test is much less sensitive than the Fain (1978) test to the number of sires. In both cases, the *hs* version is affected more by a limited number of families than the *fs* version. The *Meratfs* and *Meraths* statistics show similar tendencies even if their very low power does not permit a clear interpretation of the results.

The four test statistics derived from Famula's (1986) propositions are independent of family size (Tables 6 and 7). The major gene indexes *MGI2* (α) and *MGI3* (α)

Table 5. Effect of the number of sires on the power of the tests (%)

Test statistics	Number of sires		
	5	10	20
Bartpf	80	97	100
Bartdf	69	91	100
Meratpf	21	33	38
Meratdf	20	29	34
Fainpf	53	87	99
Faindf	14	47	91
Hanfain	11	21	31
MPCC	25	38	64
MGI2 (0.5)	8	11	14
MGI2 (1)	12	14	13
MGI2 (2)	16	18	23
MGI3 (0.5)	12	14	20
MGI3 (1)	19	23	34
MGI3 (2)	19	24	33
Famula (0.5)	13	13	25
Famula (1)	13	14	22
Famula (2)	13	12	20
Famula (4)	13	13	22
Famul1	19	25	32
Famul2	31	41	55
Famul3	15	15	16
Famul4	28	41	53

Table 6. Effect of the number of dams, with 1 progeny per dam, on the power of the tests (%)

Test statistics	Number of dams/sire		
	5	10	20
Bartdf	58	87	98
Meratdf	11	17	30
Faindf	50	74	88
MPCC	23	45	64
MGI2 (0.5)	8	11	14
MGI2 (1)	9	11	13
MGI2 (2)	15	18	23
MGI3 (0.5)	14	16	20
MGI3 (1)	21	26	34
MGI3 (2)	18	27	33
Famula (0.5)	13	6	8
Famula (1)	14	7	7
Famula (2)	15	7	8
Famula (4)	23	27	19
Famul1	23	23	27
Famul3	14	13	14

Table 7. Effect of the number of progeny per sire, with 1 progeny per dam, on the power of the tests (%)

Test statistics	Number of progeny/sire		
	5	10	20
Bartpf	64	96	100
Meratpf	10	32	38
Fainpf	52	56	92
Hanfain	10	15	17
MPCC	27	34	40
MGI2 (0.5)	8	9	11
MGI2 (1)	11	13	13
MGI2 (2)	14	17	19
MGI3 (0.5)	14	15	14
MGI3 (1)	15	21	19
MGI3 (2)	14	17	16
Famula (0.5)	19	24	25
Famula (1)	21	25	22
Famula (2)	22	26	20
Famula (4)	19	19	15
Famul1	21	23	32
Famul3	13	15	16

Table 8. Effect of the family structure on the power of the tests (%). 20 sire families, m dams/sire and d progenies/dam

Test statistics	$m=1$ $d=20$	$m=4$ $d=5$	$m=5$ $d=4$	$m=20$ $d=1$
Bartpf	100	99	97	–
Bartdf	–	100	99	98
Meratpf	38	16	13	–
Meratdf	–	34	31	30
Fainpf	92	99	99	–
Faindf	–	91	90	88
Hanfain	17	31	28	–
MPCC	40	52	54	64
MGI2 (0.5)	11	12	13	14
MGI2 (1)	13	13	13	13
MGI2 (2)	19	20	21	23
MGI3 (0.5)	14	14	17	20
MGI3 (1)	19	24	30	34
MGI3 (2)	16	20	23	33
Famula (0.5)	25	15	12	8
Famula (1)	22	13	12	7
Famula (2)	20	10	11	8
Famula (4)	15	16	22	19
Famul1	32	25	29	27
Famul2	–	48	55	–
Famul3	16	13	14	14
Famul4	–	53	52	–

are not sensitive to the number of progenies/dam, but show a 50–100% increase of their power when the number of dams/sire changes from 5 to 20. The Bartlett, Fain (1978) and also the Mérat (1968) methods are sensitive to the parameters, as are the *MPCC* statistics.

When the proportion of half sibs increases in the sample, *meratfs* and *famula* (α) (for small α values) are less

Table 9. Effect of the type of major locus on the power of the tests (%). Situations 1 to 13 are defined in Table 4

Test statistics	Situations												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Bartpf	9	62	98	17	94	78	15	100	13	18	11	76	6
Bartdf	9	52	98	10	95	50	10	100	12	5	8	56	6
Meratpf	7	8	17	32	6	18	8	21	7	16	8	38	13
Meratdf	7	8	20	6	6	18	7	30	6	9	7	34	9
Fainpf	21	38	86	22	88	47	21	99	23	39	19	99	40
Faindf	7	30	79	11	63	52	9	91	6	16	11	67	12
Hanfain	7	7	11	9	16	21	7	31	7	16	8	22	8
MPCC	10	21	38	60	17	64	34	35	7	52	1	26	15
MGI2 (0.5)	7	7	13	5	10	8	7	11	7	6	8	10	14
MGI2 (1)	6	7	15	5	13	9	5	14	7	7	8	13	13
MGI2 (2)	6	10	21	6	19	11	6	23	7	9	6	11	8
MGI3 (0.5)	6	8	14	6	17	6	5	20	7	6	5	13	7
MGI3 (1)	6	9	24	5	31	6	4	34	7	6	3	17	7
MGI3 (2)	8	8	15	6	33	6	4	27	8	7	4	12	7
Famula (0.5)	7	6	7	5	4	6	6	5	8	10	16	9	25
Famula (1)	7	6	6	5	4	5	5	4	7	9	16	10	25
Famula (2)	7	7	6	5	6	5	5	7	8	8	19	12	26
Famula (4)	7	8	9	6	27	6	5	16	8	8	17	18	19
Famul1	8	18	32	14	29	17	16	19	8	11	11	23	12
Famul2	9	22	32	46	16	48	55	24	8	15	14	11	5
Famul3	7	12	16	8	16	14	7	14	8	8	6	7	2
Famul4	11	31	53	32	26	46	35	24	10	13	12	8	6

powerful. On the other hand, *MPCC*, *MGI3* (α) and *Hanfain* appear to be more powerful. The four tests derived from Famula, as *MGI2* (α), *Meraths* and Bartlett and Fain tests, are not sensitive to family structure.

Concerning the mode of inheritance (Table 9), a central point is the deviation between genotype means. Except for *famula* (α), all the tests power increases with $\mu_3 - \mu_1$ deviation. With a difference higher than $3\sigma_1$, the Bartlett test as well as the Fain (1978) test and the *Famul4* statistic have a power greater than 50%. With a $2\sigma_1$ deviation, only the Bartlett test reaches this power, and with a σ_1 deviation none of the criteria satisfies that property. Thus, the major gene corresponding to situation 1 is practically unidentifiable.

Concerning dominance, the results are not as clear: a codominant gene is easier to detect with *SEDA* methods when the Bartlett and Fain (1978) tests are much more efficient in the dominant situation. Similary, heterogeneity of the within-genotype variances adds to the power of Bartlett and Fain tests, but decreases the usefulness of the *SEDA*. The behaviour of the three statistics *MPCC*, *Meratfs* and *Meraths* is much more difficult to understand because the effect of the dominance situation depends on the allele frequencies.

The equality of the allele frequencies helps when the gene is dominant or when the within-genotype variances are different; given the limited sample sizes studied here, the chance, when a is rare, that one of the sires shows a

Table 10. Effect of the population size on the tests level: number of H_0 rejection, at the 5% level, for 100 simulations under H_0

Test statistics	Number dams/sire	Number progenies/dam	Number of sires					
			10	20	30	40	50	100
Bartpf	4	5	7	2	3	11	2	8
	1	20	4	8	4	6	2	6
Fainpf	4	5	4	10	6	10	6	10
	1	20	1	11	10	10	11	9
Bartdf	4	5	7	5	10	6	4	2
	20	1	7	7	7	4	7	4
Faindf	4	5	5	3	5	7	8	5
	20	1	5	8	10	13	5	6

Table 11. Effect of the non-normality of the distribution on the robustness of the tests: number of H_0 rejection, at the 5% level, for 100 simulations under H_0

Test statistics	Number dams/sire	Number progenies/dam	Type of distribution[a]						
			D11	D12	D13	D2	D31	D32	D33
Bartpf	4	5	–	–	–	0	100	23	4
	1	20	–	–	–	0	100	28	6
Fainpf	4	5	–	–	–	32	100	77	34
	1	20	–	–	–	6	100	77	34
Bartdf	4	5	–	–	–	0	100	28	4
	20	1	99	2	0	0	100	47	8
Faindf	4	5		–	–	12	100	78	26
	20	1	100	100	64	2	100	92	27

[a] D11, D12, D13, discrete distributions; D2, bimodal distribution; D31, D32, D33, asymmetric distributions

distribution with a high mean (or variance) is small. On the other hand, except for *MPCC, Meraths* and *Meratfs*, the power of the criterion is not linked to the allele frequencies for a codominant gene.

When the dam population is fixed for *aa*, the frequency equilibrium is still an advantage, but for *Famula* (α). *MPCC, Meratfs* and *Meraths* appear more powerful when all the dams are *aa*. On the other hand, Bartlett and the four *famul* indicators are more powerful when both alleles are segregating in the dam population. Finally, the Fain (1978) method is not very sensitive to this effect.

Robustness

The results are given in Tables 10 (effect of the population size) and 11 (non-normality). Both tests (Bartlett and Fain), whatever their version (*fs* and *hs*), are not sensitive to the number of sires, since no increase in the number of *H0* rejection is observed when this number decreases even for the smaller numbers studied.

Deviations from normality have more heterogeneous consequences on robustness. Concerning discrete distributions (D1), both the Bartlett and Fain tests are useless for the D11 situation (only two classes), the rejection of *H0* being systematic in this case. The Fain test is still useless for situations D12 and D13, when the Bartlett test appears robust, the values being even lower, as compared to the normal case, which could indicate a loss of power. Conversely, bimodality due to the environment has a similar but much lighter effect; no error for the Bartlett test, up to 32% errors for the Fain (1978) criteria.

Finally, the asymmetry of the distribution is a very important source of false *H0* rejections, in particular for the Fain (1978) statistics.

Discussion and conclusions

With the family sizes studied here, we confirm the positive results of Fain (1978) concerning *Bartlett* and *Fain*, which cannot be compared to the negative results of MacCluer and Kammerer (1984), obtained with much smaller family sizes.

On the other hand, we do not confirm the superiority of *Fain* over *Bartlett* for dominant genes, as described by Fain (1978), our results showing no systematic tendency. Mayo et al. (1980) found an important loss of power of Fain when the variance within the heterozygous genotype *Aa* is smaller than the variance within *AA* or *aa*. We obtained the opposite result when the variance within *AA* is higher than the others.

Concerning the *SEDA*, we confirm the relative quality of *MGI* for detection of frequent and additive genes (Karlin et al. 1981; Morton et al. 1982). On the other hand, the low performance of *MPPC* mentioned by Morton et al. (1982) cannot be considered here as systematic, the power of this test varying largely with the type of gene studied (from 1% to 64%).

Finally, we confirm the poor value of Mérat's test (1968) as evaluated by Hammond and James (1970). This could indicate that the population studied by Mérat (1971) was quite atypical.

Concerning the power, four tests may be retained for widespread use: *Bartlett, Fain, MPCC* and *Famul4*. The first two are powerful for limited number of sires and very powerful for 20 sires and 20 progenies/sire. They are fully able to detect dominant major genes, or major genes showing a more variable distribution within the favourable homozygous population. On the other hand, *MPCC* and *Famul4* need at least 20 sire families in order to get a power over 50% and are particularly suited to additive gene with equal within-genotype variances.

The robustness of the two more powerful tests (*Bartlett* and *Fain*) is limited, which could limit their usefulness, in particular when the trait is not normally distributed (a situation naturally observed in the global distribution when a major gene is effectively segregating

in the population). Our conclusions are similar to Fain's (1978) results. Fain, when simulating human populations (one mother/father, four children/family), found a low robustness for both methods and better behaviour of *Bartlett*. Following Fain (1978), a normalization of the data before the analysis may improve the robustness, but results in an important loss of power (about 50%).

If these test statistics are to be largely used as first indicators of a major gene segregation, eventual positive results would have to be confirmed and detailed with more sophisticated methods such as the use of recombinant DNA technology and the ML methods (Mayo 1989).

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