STUDY ON GENETIC VARIANCE BETWEEN MARKERS AND ITS EXPECTATION FOR A CENTRAL OR TERMINAL MARKER IN AN F2 POPULATION

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SUMMARY

An index relevant to the experimental power of marker-QTL detection is \( V_b/(V_p-V_b) \). Maximum value of \( V_b/V_q \) can only be achieved by finding the most appropriate marker. \( E(V_b/V_q) \) is a function of number, degree of dominance and configuration of QTL, marker position, and chromosome length. When a marker was linked to one or two cis-configurated segregating QTL, \( E(V_b/V_q) \) decreased rapidly with longer chromosomes, while a nonlinear relationship between the length and \( E(V_b/V_q) \) was observed in QTL trans-configuration. \( E(V_b/V_q) \) of a central marker is generally larger than that of a terminal one. \( V_b \) and \( V_q \) generally increased in the presence of complete dominance. Trans-configuration of QTL dramatically reduced the value of \( V_b \), \( V_q \) and the maximum value of \( V_b/V_q \), which greatly increases the difficulty of the marker-QTL detection.

INTRODUCTION

The value of DNA polymorphic fragments as genetic markers is determined by degree of polymorphism, availability, and distribution over the genome. In reality, highly polymorphic markers are not readily obtainable, and scoring them individually is a time- and resource-consuming process. In addition, some highly polymorphic markers such as variable number of tandem repeats (VNTR) tended to be organized in clusters, especially at proterminal regions (Georges et al., 1990).

Dekkers and Dentine (1991) studied the expected variance between markers, \( E(V_b) \), in a segregating population. Their analytical results indicated that as a marker departed from the central location on a chromosome with a QTL located anywhere with equal probability, \( E(V_b) \) was reduced.

THEORY AND RESULTS

Consider a chromosome of length \( L \) Morgans with a polymorphic marker located \( L_1 \) and \( L_2 \) Morgans from two ends of the chromosome \( (L_1 + L_2 = L) \). Assume one or two QTL are segregating on the chromosome, and the QTL can be located anywhere on the chromosome with equal probability. If map distances are proportional to physical distances, the QTL are uniformly distributed over the chromosome, and the density function is equal to \( 1/L \) for one QTL and \( 1/L^2 \) for two QTL.

\[ F_2 \] progeny were generated by inter se mating \( F_1 \) progeny, which came from a cross between two completely inbred lines. The determination of the genotype of \( F_2 \) progeny involves multiple linked loci, and the recombination fraction \( r \) for a map distance \( x \) between any two loci is calculated using Haldane's (1919) mapping function, \( r = 0.5(1-e^{-2x}) \), which assumes no interference. The probability of crossing over during meiosis between any contiguous loci on a chromosome is equal to \( 2r \), which permits calculation of genetic variance between and within markers (Falconer, 1989).

One QTL

The genetic variance between markers \( (V_b) \), total genetic variance resulting from the segregation of the QTL under study \( (V_q) \) and the expectation of the ratio of \( V_b \) to \( V_q \) are given by:
\[ V_b = 0.5(e^{-4x_1}a_2^2) + 0.25(e^{-8x_2}d_2^2) \]  
\[ V_q = 0.5a_2^2 + 0.25d_2^2 \]

\[ E \left( \frac{V_b}{V_q} \right) = \frac{4a_2^2(2-e^{-4L_1}e^{-4L_2}) + d_2^2(2-e^{-8L_1}e^{-8L_2})}{L(16a_2^2 + 8d_2^2)} \]

where \[ a, d \] and \[ -a \] are the genetic effects of QTL genotypes \[ QQ, Qq \] and \[ qq, \] respectively.

Equations (1) and (2) show that the maximum value of \[ V_b \] is equal to \[ V_q \]. \[ E(V_b/V_q) \] is a function of the ratio of genetic effect of the QTL to degree of dominance \((a/d)^2\), marker position \((L_1/L)\), and the length of the chromosome \((L)\) (Equation (3) and Figure 1). \[ E(V_b/V_q) \] decreased rapidly with increasing chromosome length. A central polymorphic marker \((L_1/L = 0.5)\) resulted in approximately 15% higher \[ E(V_b/V_q) \] than a terminal marker \((L_1/L = 0.1)\). When a favorable allele exhibited complete dominance to its unfavorable allele, \[ E(V_b/V_q) \] decreased substantially. However, it is noted that \[ V_b, E(V_b), \] and \[ V_q \] increased with the presence of complete dominance compared to no dominance (Equations (1) and (2)).

**Two QTL**

When no interaction is assumed between two QTL, the values of \[ V_b, V_q \] and \[ E(V_b) \] can be written as:

\[ V_b = 0.5(a_1e^{-2x_1}+a_2e^{-2x_2})^2 + 0.25(d_1e^{-4x_1}+d_2e^{-4x_2})^2 \]  
\[ V_q = 0.5(a_1^2+a_2^2+2e^{-2y}a_1a_2) + 0.25(d_1^2+d_2^2+2e^{-4y}d_1d_2) \]

\[ E(V_b) = \frac{1}{L^2} \left\{ \frac{a_1^2+a_2^2}{8}(2-e^{-4L_1}e^{-4L_2})(L_1+L_2) + \frac{a_1a_2}{4}(2-e^{-2L_1}e^{-2L_2})^2 \right\} \]

\[ + \frac{d_1^2+d_2^2}{32}(2-e^{-8L_1}e^{-8L_2})(L_1+L_2) + \frac{d_1d_2}{32}(2-e^{-4L_1}e^{-4L_2})^2 \]

where \[ a_1, -a_1, d_1, a_2, -a_2, \] and \[ d_2 \] are the genotypic values of QTL genotypes \[ Q_1Q_1, q_1q_1, Q_1q_1, Q_2Q_2, q_2q_2, \] and \[ Q_2q_2, \] respectively, and \[ x_1, x_2, \] and \[ y \] are the map distances between marker locus and two QTL, and between two QTL, respectively.

All numerical evaluations are based on the assumption that the absolute size of genetic effect and degree of dominance of two QTL are equal. The evaluation of \[ E(V_b/V_q) \] is numerically illustrated for the case when two linked QTL occur in a cis-configuration (Figure 2). \[ E(V_b/V_q) \] decreased rapidly as the chromosome length increased. \[ E(V_b/V_q) \] of a central marker is decreased from \(0.88\) to \(0.15\) for no dominance \((d = 0)\), and from \(0.84\) to \(0.12\) for complete dominance \((d = a)\) as the length of the chromosome increased.
chromosome increased from .2 to 4.0 Morgans, which is slightly larger than observed in the case of one QTL. A terminal marker resulted in approximately 15% lower E(Vb/Vq) than a central marker. The presence of complete dominance resulted in slightly smaller E(Vb/Vq) than absence of dominance. However, the value of Vb, Vq and E(Vb) increased with the presence of dominance (Equations (4) to (6)).

Trans-configuration of two linked QTL dramatically reduced the value of Vb, Vq (Equations (4) and (5); Figure 3). A nonlinear relationship between E(Vb/Vq) and L was observed. E(Vb/Vq) of a central marker increased from .02 to .11, but reduced to .08 as the length of the chromosome increased from .2 to 1.4 and to 4.0 Morgans in the case of no dominance, respectively. There was a slightly positive effect on E(Vb/Vq) when the marker locus position was changed from central to terminal. When the favorable alleles exhibited complete dominance to their unfavorable alleles in two trans-configurated QTL, the value of Vb, Vq and E(Vb/Vq) increased considerably.

The maximum value of Vb/Vq, which can be achieved by finding the most appropriate marker, is a function of QTL configuration, the recombination fraction between two QTL (r) and the degree of dominance (Figure 4, dominance data not shown). The maximum value of Vb/Vq decreased from 1 to .5 in QTL cis-configuration and increased from 0 to .5 in trans-configuration as r changed from 0 to .5, respectively. Therefore, QTL configuration status has a more dramatic impact when QTL are more tightly linked.

DISCUSSION

An approximate measurement of the efficiency of marker-QTL association detection is Vb/Vq. Larger values of E(Vb/Vq) of a marker indicates that the marker is generally more valuable. Only the most appropriate marker can achieve the maximum value of Vb/Vq. Large differences between the values of Vb/Vq of an ideal and an actual marker generally implies that the marker-QTL detection can be improved by finding a more appropriate marker. Position of a marker is a more important factor and more polymorphic marker loci are needed in order to map the QTL efficiently if the difference between Vb/Vq of a marker and the maximum Vb/Vq is large.

It is noted that Vb/(Vp-Vb) is an index relevant to the experimental power of detection of QTL, where Vp is the phenotypic variance of the trait under study. Factors such as complete dominance of QTL, which increases Vb and Vq of a marker as well as Vb/(Vp-Vb) in general, will often facilitate the marker-QTL detection, while other factors such as trans-configuration of multiple linked QTL, which dramatically reduces the value of Vb, Vq, and Vb/Vq, can considerably increase the difficulty of marker-linked QTL detection. As a result, building or choosing an appropriate linkage disequilibrium population such as lines or families with cis-configurated linked QTL is equally important as finding a large number of highly polymorphic marker loci in marker-QTL detection.

REFERENCES

Figure 1. Expected genetic variance between markers of \( V_J \) to genetic variance \( V_q \) in an F2 population for a marker located \( L_j \) Morgans from the end of a chromosome \( L \) Morgans long with 1 QTL. A: \( L_j/L = .5 \), no dominance; B: \( L_j/L = .5 \), complete dominance; C: \( L_j/L = .1 \), no dominance; D: \( L_j/L = .1 \), complete dominance.

Figure 2. Expected ratio of \( V_b \) to \( V_q \) in an F2 population for a marker linked to 2 cis-configurated QTL and located \( L_j \) Morgans from an end of a chromosome \( L \) Morgans long. A: \( L_j/L = .5 \), no dominance; B: \( L_j/L = .5 \), complete dominance of favorable alleles of 2 equal-sized QTL to their unfavorable alleles; C: \( L_j/L = .1 \), no dominance; D: \( L_j/L = .1 \), complete dominance from favorable alleles of 2 QTL to their unfavorable alleles.

Figure 3. Expected ratio of \( V_b \) to \( V_q \) in an F2 population for a marker linked to 2 trans-configurated QTL and located \( L_j \) Morgans from an end of a chromosome \( L \) Morgans long. A: \( L_j/L = .5 \), no dominance; B: \( L_j/L = .5 \), complete dominance of favorable alleles of 2 equal-sized QTL to their unfavorable alleles; C: \( L_j/L = .1 \), no dominance; D: \( L_j/L = .1 \), complete dominance from favorable alleles of 2 QTL to their unfavorable alleles.

Figure 4. \( V_q \) and the ratio of \( V_b/V_q \) for a marker with maximum \( V*/V_q \) and linked to 2 QTL in an F2 population. Genetic effects of both QTL were assumed equal to 1 with no dominance. A: \( V_q \) curve, 2 QTL cis-configurated; B: \( V_b/V_q \) curve, 2 QTL cis-configurated; C: \( V_q \) curve, 2 QTL trans-configurated; D: \( V_b/V_q \) curve, 2 QTL trans-configurated.