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Trait-based analyses for the detection of linkage between marker loci and quantitative trait loci in crosses between inbred lines*

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Summary. Methods are presented for determining linkage between a marker locus and a nearby locus affecting a quantitative trait (quantitative trait locus = QTL), based on changes in the marker allele frequencies in selection lines derived from the F-2 of a cross between inbred lines, or in the "high" and "low" phenotypic classes of an F-2 or BC population. The power of such trait-based (TB) analyses was evaluated and compared with that of methods for determining linkage based on the mean quantitative trait value of marker genotypes in F-2 or BC populations [marker-based (MB) analyses]. TB analyses can be utilized for marker-QTL linkage determination in situations where the MB analysis is not applicable, including analysis of polygenic resistance traits where only a part of the population survives exposure to the stressor and analysis of marker-allele frequency changes in selection lines. TB analyses may be a useful alternative to MB analyses when interest is centered on a single quantitative trait only and costs of scoring for markers are high compared with costs of raising and obtaining quantitative trait information on F-2 or BC individuals. In this case, a TB analysis will enable equivalent power to be obtained with fewer individuals scored for the marker, but more individuals scored for the quantitative trait. MB analyses remain the method of choice when more than one quantitative trait is to be analyzed in a given population.

Key words: Quantitative trait – Genetic markers – QTL – Linkage analysis – QTL mapping

Introduction

Methods for locating chromosomal regions or loci affecting quantitative traits (quantitative trait loci = QTL) based on their linkage relations to Mendelian marker loci have been presented by Thoday (1961) and applied in experimental and agricultural species (Kluge and Geldermann 1982; Law 1966; Patterson et al. 1968; Spickett and Thoday 1966; Tanksley et al. 1982; Weller 1983; Vallejos and Tanksley 1983; Zhuchenko et al. 1979). Marker-QTL linkage information of this sort can find useful application in applied breeding programs (Beckmann and Soller 1983, 1986a, b; Burr et al. 1983; Tanksley and Rick 1980; Soller and Beckmann 1982, 1983, 1985; Tanksley and Orton 1983).

The above studies are all based on differences, generated by QTL linked to the marker locus, in the mean value of a quantitative trait between marker genotypes in the F-2 or backcross (BC) of a cross between inbred lines. An alternative approach, suggested by Stuber et al. (1980, 1982), is to examine marker allele frequencies in selected lines originating from a cross between inbred lines. In such populations, selection would be expected to change allelic frequencies of segregating plus or minus alleles at QTL affecting the trait in question, increasing the frequency of plus alleles in the high line and the frequency of minus alleles in the low line. Hitchhiker effects between such QTL alleles and nearby marker alleles would be expected to generate corresponding changes in the allelic frequencies of the coupled marker alleles. Consequently, marker loci at which allele frequencies differed significantly in the high and low selection lines would be considered to be in linkage to QTL having an effect on the trait under selection. In this way, the number of segregating QTL affecting the trait under selection and their general map locations would be determined.

There are a number of situations in which the Stuber type of analysis [trait based (TB) analysis] can prove more useful than the Thoday analysis [marker-based (MB) analysis]. All of these situations involve experimental designs where the analysis is aimed primarily at a single quantitative trait. These

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include: Design (i), analysis of an F-2 or BC population in which only a part of the population may survive after exposure to a stressor, such as high salinity, temperature extremes, drought and disease. Design (ii), analysis of selection lines initiated by a cross between inbred lines. This design would apply even in the initial stages of selection, before fixation is reached for the QTL involved in the selection response. Design (iii), general analysis of an F-2 or BC population for a particular quantitative trait, when costs of scoring for markers are appreciably higher than the costs of raising progeny and scoring them for the trait, e.g., as in the initial stages of a plant pedigree breeding program or in the initial generations of a synthetic animal population formed by crossing two breeds.

Designs (i) and (iii) differ from (ii) in that they involve an F-2 population between two inbred lines or between a cultivar and a landrace, whereas (ii) involves selected lines originating from an F-2. Design (i) differs from (iii) in that (i) involves the analysis of the one surviving tail of a population only, whereas (iii) involves both phenotypic tails of a population. Note that the phenotypically extreme classes of Designs (i) and (iii) can be considered to be the equivalent of the first parental generation of a selection experiment. Consequently, Designs (i) and (iii) are actually cases of Design (ii), Design (i) being the equivalent of one cycle of a selection experiment carried out in one direction only, i.e., a one-step, one-way selection experiment, while Design (iii) is the equivalent of one cycle of a divergent selection experiment i.e., a one-step, two-way selection experiment.

In the present study, the properties of TB analyses appropriate to the above situations are considered and compared, when relevant, with the corresponding MB analysis.

Theory

Experimental designs for a trait-based analysis

A TB analysis can take a number of experiment forms, depending on the situation investigated, as follows:

Design (i). For analysis of resistant loci, a large F-2 or BC population would be formed and exposed to the stressor. Marker allele frequencies would then be determined in the survivors and compared with the expected Mendelian frequencies (normally, 0.5 for an F-2 population, 0.75 or 0.25 for a BC population). Marker alleles showing allelic frequencies that differed significantly from expectation would be scored in an unselected population to test for possible segregation distortion. In the absence of such effects these marker loci would be considered to be in putative linkage with QTL affecting the resistance trait.

Design (ii). For analysis of lines originating from a cross between inbred lines and selected in one direction only, marker frequencies in the selection lines would be compared with the expected F-2 frequency of 0.5; when lines are available that originated from the same F-2, but were selected divergently, marker frequencies in the high and low selection lines would be compared.

Design (iii). For general analysis of quantitative traits, an F-2 or BC population would be evaluated for the quantitative trait and marker allele frequencies scored and compared in the phenotypically extreme high and low tails of the population. This would exploit the ability of TB analyses to conserve scoring for markers at the expense of increased scoring for the quantitative trait. A significant deviation of observed from expected marker frequencies or a significant difference in marker allele frequencies between high and low selection classes or lines would be an indication of linkage between the marker locus exhibiting the deviant frequencies and a QTL affecting the trait in question.

Change in marker allele frequencies in selection classes or lines

As pointed out above, the survivors of a Design (i) experiment and the extreme phenotypic classes of a Design (iii) experiment can be considered the equivalent of the selected parent classes of a one-step selection experiment. Thus, the term "selected classes" will be used as an inclusive term for the above phenotypic classes as well as for the actual Design (ii) selection classes. Changes in marker allele frequencies in the selected classes will be generated by hitchhiker effects due to the primary change in gene frequencies at the linked QTL resulting from the phenotypic selection applied. These changes in marker allele frequencies can be calculated in the following manner.

Let A_1 and A_2 denote alleles at a locus affecting a quantitative trait. Within each of the three genotypic classes, A_1A_1, A_1A_2 and A_2A_2, the quantitative character is assumed to be normally distributed with standard deviation σ_w, and means d, h and $-$ d, respectively. It is assumed that the locus A contributes only a small part of the total phenotypic variance of the population so that σ_w is approximately equal to σ, the overall phenotypic standard deviation of the population. At the marker locus the alleles are denoted M_1 and M_2 and it is assumed that the three marker genotypes have distinguishable phenotypes. Initially we assume complete fixation of alternative alleles in two inbred lines: Line 1 with genotype M_1A_1/M_1A_1 and Line 2 with genotype M_2A_2/M_2A_2

Following Falconer (1981, p. 185), the difference in allelic frequencies at a QTL as a result of a one-step, two-way selection carried out in an F-2 population will equal

$$\delta_{A,F\text{-}2} = i_P D/4$$

where,

D = 2 d/σ is the proportional effect at the QTL (Falconer 1981);
P = the proportion of the total population included in the selected class, and
i_P = the standardized selection differential (Falconer 1981) between the high (or low) selection class of the population and the population mean.

i_P as a function of P can be obtained from the expression given by Falconer (1981, p. 176) or from appropriate tables (Becker 1967).

In a similar manner it can be shown that for a BC population, assuming h = 0, the change in allele frequencies at a QTL as a result of a one-step, two-way selection will be

$$\delta_{A,BC} = i_P D/8 .$$

The change in allele frequencies at the QTL as a result of t cycles of selection initiated in an F-2 population will be approximately $t\,\delta_{A,F\text{-}2}$, for small t. The corresponding change in allele frequencies at a marker locus, generated by hitchhiker effects due to changes in frequency at a linked QTL will be

$$\delta_{M,1} = (1 - 2r)\,\delta_{A(F\text{-}2 \text{ or } BC)} \text{ for one selection step,}$$

where

r = the proportion of recombination between QTL and marker locus

and

$$\delta_{M,t} = \sum_{j=1}^{t} (1 - 2r)(1 - r)^{j-1} \delta_{A\,(F\text{-}2 \text{ or } BC)}$$

for t cycles of selection ignoring terms of the order δ_A^2.

Standard errors of changes or differences in marker allele frequencies

To determine the statistical significance of observed deviations or differences in marker allele frequencies, it is necessary to compare the estimate with its standard error. For a comparison of an observed marker allele deviation in a one-way, one-step selection experiment with some expected Mendelian value, this is given by the standard error of a binomial proportion,

$$\text{S.E. } (\delta_M) = (m_1 m_2/PT)^{0.5}$$

where

m_1 and m_2 are marker allele frequencies, assuming symmetrical changes in the high and low selection classes, and

T is the total population size.

For a comparison of the observed difference in marker allele frequencies between high and low selection classes in a one-step, two-way experiment,

$$\text{S.E. } (\delta_M) = (2\, m_1 m_2/PT)^{0.5}.$$

Ignoring changes in marker allele frequencies, standard errors for t generations of selection, will equal

$$\text{S.E. } (\delta_{M,t}) = t^{0.5}(\text{S.E. } \delta_M).$$

Experiment size

We now consider the total population size required to detect a marker allele frequency change or difference, with Type I error, α, and Type II error, β. This will be the population size that satisfies the relation

$$\delta_M/\text{S.E. } (\delta_M) = z_\alpha + z_\beta \qquad (1)$$

where,

z_α and z_β are the standardized normal curve ordinates for α and β, respectively.

Table 1 summarizes the expected changes in marker allele frequencies and their standard errors for various cases. In deriving these expressions, appropriate note was taken of the fact that the Mendelian expectation for marker allele frequencies in an F-2 and BC population are $m_1 = m_2 = 0.5$ and $m_1 = 0.75$, $m_2 = 0.25$, respectively; also, that in one-way selection, observed marker frequencies, having a standard error, are compared with Mendelian expectations which do not have standard errors, while in two-way selection analyses two observed frequencies are compared, both of which have standard errors.

For the one-step, two-way F-2 selection experiment, substitution of the appropriate expressions for δ_M and S.E. (δ_M) from Table 1 in expression (1) and solving for T, gives

$$T = 2(z_\alpha + z_\beta)^2/\delta^2{}_M P.$$

Required population sizes for the other experimental situations, calculated in a similar manner, turn out to be simple multiples of the above, and the appropriate factors are also shown in Table 1.

Effect of proportional effect of the quantitative locus, recombination and incomplete fixation on experimental size

Examination of the above expressions shows that experiment size required for given power will be inversely proportional to the square of the proportional effect of the locus. Consequently, loci having large effects can be detected with relatively small numbers. The effect of recombination is to shift D to an effective value of $(1 - 2r)^2 D$ (Soller et al. 1976). Similarly, incomplete fixation of alleles will decrease the proportional effect of the QTL that is associated with marker genotypes in MB analyses, and decrease the change in marker-allele frequencies associated with high and low selection classes in TB analyses. The decrease will depend on the degree of incomplete fixation and is expressed in the power curves as an equivalent shift to the left along the D axis from D to $(m_{11} - m_{21})(a_{11} - a_{21})D$, where m_{11} and m_{21} are allelic frequencies for marker allele M_1 in Lines 1 and 2, respectively, and a_{11} and a_{21} are corresponding allelic frequencies at the QTL in the two lines (Soller et al. 1976). As pointed out above, small changes in D can have large effects on power of this test. Thus, recombination and incomplete fixation can have major effects on the size of experiment required for given power, depending on the proportional effect at the quantitative locus.

Effect of including additional traits in a TB analysis

Two or more traits can be included in a TB analysis of an F-2 or BC population by subjecting the same population to independent selection with respect to each trait or by choosing the selected classes on the basis of an index combining values for both traits simultaneously. Independent selection will require scoring almost twice as many individuals for the markers as in the case of a single trait (there will be some saving in the number of individuals scored for the marker due to those individuals that score high (or low) for both traits). As will be evident from the "Numerical results" section (Table 2), this would involve many more individuals scored for the quantitative traits and, except at the very lowest values of P, substantially more total marker determinations than the corresponding MB analysis. Index selection with respect to k traits would reduce the effective intensity of selection against each individual trait in the index to $i/\sqrt{k}$, reducing δ_M by an equivalent amount. Since experimental size for given power is inversely related to δ_M^2, this means, e.g. that for index selection with respect to two traits, experimental numbers will have to be doubled in order to have power for each trait equivalent to that obtained with a comparable proportion-selected applied to a single trait. Again, the end result would be more quantitative trait and marker determinations than required by the corresponding MB analysis.

When an index is used as a means of including two or more traits in a selection program, the change in marker gene frequencies as a result of selection will again the proportional to $i\sqrt{k}$, where k is defined as above, and experiment size for given power will have to be increased k-fold, as compared to single-trait selection. In this case consideration of Table 3 shows that index selection for two traits may still offer some reduction in number of individuals scored for the markers, depending on the proportion of selection and the proportion of recombination between marker locus and QTL. Nevertheless, in contrast to MB analyses, which can deal simultaneously with as many quantitative traits as it is convenient and useful to measure on the experimental populations, it seems fair to conclude that TB analyses are limited in practice to situations where a single trait is of interest.

Table 1. Expressions for expected change in marker allele frequencies in a one-step, two-way F-2 selection experiment as a result of changes due to selection at linked QTL, as a function of proportion selected (P), proportional effect of the QTL (D) and likelihood of recombination (r). Also shown are expressions for standard error of the change in marker allele frequencies, total population size required to detect these changes with given Type I error (α) and Type II error (β), and total numbers scored for markers. Values for the other experimental designs are given as multiples of the expressions for the one-step two-way F-2 experiment

Type of experiment	Allele frequency change at		S.E.	Total population size (T)	Total no. scored for markers
	QTL	Marker locus			
F-2					
One-step, two-way	$i_P D/4$	$(1-2r)\,\delta_A$	$(1/2\,PT)^{0.5}$	$\frac{(z_\alpha + z_\beta)^2}{2P(\delta_M)^2}$	$2PT$
In multiples of the F-2 expressions					
One-step, one-way	1/2	1/2	$(1/2)^{0.5}$	2	1
t-steps, two-way	t	$\sum_{j=1}^{t}(1-2r)(1-r)^{j-1}$	$(t)^{0.5}$	$\frac{t^2}{\left[\sum_{j=1}^{t}(1-2r)(1-r)^{j-1}\right]^2}$	$\frac{t}{\left[\sum_{j=1}^{t}(1-2r)(1-r)^{j-1}\right]^2}$
t-steps, one-way	t	$(1/2)\sum_{j=1}^{t}(1-2r)(1-r)^{j-1}$	$(t/2)^{0.5}$	$\frac{2t^2}{\left[\sum_{j=1}^{t}(1-2r)(1-r)^{j-1}\right]^2}$	$\frac{t}{\left[\sum_{j=1}^{t}(1-2r)(1-r)^{j-1}\right]^2}$
Backcross					
Two-way	1/2	1/2	$(3/8)^{0.5}$	3	3
One-way	1	1	$(3/4)^{0.5}$	6	3

1 See text for details
2 Notation: i_P = intensity of selection corresponding to a proportion selected, P; t = number of cycles of selection; z_α, z_β ordinates of the normal curve corresponding to likelihoods α and β of Type I and Type II error, respectively; δ_A, δ_M defined in text.
3 Abbreviations: QTL = quantitative trait locus.

Table 2. The expected change in marker allele frequency, total population size required and total numbers scored for the marker for the one-step, two-way F-2 trait-based selection experiment, as a function of the proportion selected (P), for Type I error $\alpha = 0.05$ and Type II error $\beta = 0.20$ and assuming proportional effect, D = 0.2 and proportion of recombination r = 0. Total numbers required for the corresponding marker-based experiment are also shown

Proportion selected	Change in marker allele frequency	Total population size	Total nos. scored for markers
0.01	0.27	22,077	442
0.05	0.21	7,368	737
0.10	0.18	5,090	1,018
0.15	0.16	4,329	1,299
0.20	0.14	4,000	1,600
0.25	0.13	3,883	1,941
0.27	0.12	3,869	2,090
0.30	0.12	3,890	2,334
0.35	0.11	4,002	2,802
0.40	0.10	4,200	3,361
0.45	0.09	4,500	4,050
0.50	0.08	4,925	4,925
Marker based			1,568

Numerical results

The total number, T, of individuals in the one-step, two-way F-2 experiment that must be scored for the quantitative trait in order to achieve Type I and Type II errors, $\alpha = 0.05$, $\beta = 0.20$, respectively, are given in Table 2 as a function of the proportion selected, P, for the case D = 0.2, r = 0. Also shown in Table 2 are the expected change or difference in marker frequencies in each case, and the total number of individuals that must be scored for the markers. Values for other types of analysis can be obtained by multiplying the values in Table 2 by the appropriate factors given in Table 1. Values for $\alpha = 0.01$ will be 60% greater than those in Table 2, values for $\alpha = 0.01$, $\beta = 0.10$ will be 100% greater. Since the required T is inversely proportional to D^2, offspring numbers required in order to detect loci having proportional effects, D, other than $D_0 = 0.2$ can be obtained simply by multiplying the values in Table 1 by $(0.2/D)^2$.

Table 2 shows that $P = 0.27$ requires the smallest total population size for the given Type I and Type II

errors. This is generally true for all α, β and D. For a given total sample size, scoring more than the optimum proportion of the population will reduce accuracy! This surprising result is a consequence of the following considerations. As shown in the section Theory, power of the TB analysis will be a function of δ_M/S.E. (δ_M). Although both δ_M and S.E. (δ_M) will decrease as the proportion selected, P, increases; their rate of change with P will not be the same. Thus, for TB analyses, at all values of α and β, there will be an optimum P for which the above ratio will be at a maximum. It is this value $P = 0.27$ which gave the smallest total population size in Table 2. Examination of Table 2 shows, however, that the optimum is rather broad, and total population size remains within about 10% of the optimum in the range $P = 0.15$ to 0.45. Optimum P would clearly be the proportion of choice to use in those situations where a MB analysis is not feasible, i.e., in analyzing resistance traits and the initial stages of selection lines, and when costs of scoring for the quantitative trait and for the marker are roughly equivalent.

The TB design may be employed to reduce the number of markers scored, at the expense of scoring additional offspring for the quantitative trait. However, selection proportions rather far from the optimum must be employed in order to achieve appreciable reductions in the number of offspring scored for the markers. This is due to the fact the TB design, which simply classifies phenotypes as "high" or "low", is intrinsically less powerful than the MB design which also takes into account the exact quantitative value of the various phenotypes. Consequently, at all values of P, for equivalent α and β errors, larger F-2 populations must be raised for the TB analysis as compared with the MB analysis. This is true even for the optimum P; while at $P = 0.50$, when the entire population is scored for both quantitative trait and marker alleles (providing the same amount of information as in an MB experiment) three times as many individuals need to be scored for equivalent power when the data are analyzed using a TB design as when using a MB design. It is only for $P \leqq 0.20$ that fewer F-2 individuals need to be scored for the markers in the TB as compared with the MB analysis and significant savings are not obtained until $P = 0.10$. At this proportion, over three times as many total individuals must be raised and scored for the quantitative trait as in the corresponding MB experiment, in order to realize a saving of about one-third of the individuals scored for the marker traits. At $P = 0.05$, five times as many offspring must be scored for the quantitative traits as in the MB experiment, but only half as many scored for the markers. Nevertheless, depending on the species involved, the quantitative trait under consideration and the type of marker chosen, this may represent a savings in cost and time. It should be pointed out that in addition to the TB analysis carried out on the F-2 population as a whole, it will also be possible to carry out an independent MB analysis within each of the F-2 selected classes. Thus the overall power of the experiment will be determined by the combined power of the TB analysis and the two independent MB analysis carried out on each selected-class. Because of the small number of individuals in each selected class, the power of each of the independent MB analyses will be low. Taken together, however, they could make an appreciable contribution to overall power, and might allow total experimental sizes to be reduced somewhat. This aspect of TB designs remains to be explored in detail.

In both TB and MB experiments, many markers will generally be tested for linkage to QTL but only a few true linkages are expected for any particular quantitative trait. Thus, the rather large Type I error chosen in Table 2 means that the first screening for marker-QTL linkages, using the experimental sizes given in this Table, will include a relatively large number of spurious effects. It is assumed that in most practical situations, an initial screening for marker-QTL linkage woud be followed by a second experiment intended to confirm any observed effects. This should weed out most of the spurious linkages. Despite the relatively large α error assumed in Table 2, good power for the TB design requires a relatively large F-2 population.

Table 3 shows the effect of recombination and of more than one cycle of selection for the quantitative trait on expected frequencies of the marker allele, and on the population size required for the various types of experiment. Values are given as a multiple of those obtained for a one-step two-way F-2 selection for the case $r = 0$, $\alpha = 0.05$, $\beta = 0.20$, as given in Table 2. It is apparent that for recombination values close to 0 additional cycles of selection do provide a major decrease in the total population size required each selection cycle, and in the total number of individuals scored for the markers, as compared to a single selection cycle. At $r = 0.1$, the optimum number of cycles is $t = 14$. At this value of t, population size in each generation (and hence numbers scored for the markers in the last generation of selection) required for designated power will be only 23% of that required in the one-step selection case. Of course, total populations raised over the entire number of selection cycles is greater, in this case by 5.02, than that required for a single cycle. For $r = 0.1$ and values of t greater than 14, the increase in marker allele frequency is overshadowed by the increase in S.E., and total population size required in each cycle increases. The optimum is very broad, however, and at $t = 5$, for example, the number scored

Table 3. Changes in gene frequency at the marker locus, standard errors of the changes, total population size required summed over all selection cycles, and total numbers scored for the marker for the two-way selection experiment, as a function of number of cycles of selection (t) and proportion of recombination (r). Other assumptions as in Table 2. Values are given as a multiple of those for the corresponding one-step experiment at r = 0

Proportion of recombination	No. of cycles	Change in marker allele frequency	Standard error	Total population size[1]	Total scored for markers
0.0	1	1.00	1.00	1.00	1.00
	2	2.00	1.41	1.00	0.50
	5	5.00	2.23	1.00	0.20
0.1	1	0.80	1.00	1.56	1.56
	2	1.52	1.41	1.72	0.86
	3	217	1.73	1.91	0.64
	4	2.75	2.00	2.11	0.53
	5	3.28	2.23	2.32	0.46
	6	3.75	2.45	2.56	0.43
	8	4.56	2.83	3.09	0.39
	10	5.21	3.16	2.68	0.37
	12	5.77	3.46	4.32	0.36
	14	6.24	3.74	5.02	0.36
	16	6.63	4.00	5.82	0.36
	18	6.94	4.24	6.72	0.37
	20	7.20	4.47	7.73	0.39
0.2	1	0.60	1.00	2.78	2.78
	2	1.08	1.41	3.40	1.70
	3	1.46	1.73	4.18	1.40
	4	1.77	2.00	5.10	1.28
	5	2.02	2.23	6.11	1.22
	6	2.21	2.45	7.34	1.22
	7	2.37	2.65	8.72	1.25
	8	2.50	2.83	10.28	1.28

[1] Summed over all cycles of selection

for markers will be 29% of that required for the one-step case, while total numbers are only 2.32 as great.

For r = 0.2, the optimum number of selection cycles is 5–6 and population sizes per cycle at the optimum are 44% of those for a single cycle, with corresponding savings in markers scored in the last selection cycle. Thus, in most cases, for close to maximum savings, it will pay to score for marker allele changes about five to six generations into a selection program.

Discussion

The results of this study show that TB analyses should prove a useful alternative to MB analyses for the detection of linkage between marker loci and QTL for resistance and other traits in which only a selected portion of the population remains after exposure to the stressor. Linkage analyses of this sort are useful in determining the specific genetic architecture of quantitative traits and are the first step in the implementation of marker-assisted introgression programs (Beckmann and Soller 1986b; Soller and Plotkin-Hazan 1978; Tanksley and Rick 1982). Thus, in genetic improvement programs, TB analyses would be particularly suited for analysis of a resource strain with respect to a commercial strain with a view to possible introgression of a specific quantitative trait (e.g. salt-, drought-, temperature- or disease-resistance) from the resource strain to the cultivar. Marker-assisted introgression is essential for a polygenic resistance trait, since selection will be relatively ineffective in maintaining high frequencies of the introgressed trait during the backcross generations. Marker-assisted introgression will be highly useful for monogenic recessive resistance traits, since it will be otherwise necessary to intercalate a selfing step between each backcross generation in order to allow for expression and selection of the introgressed trait. Marker-assisted introgression can also be useful in case of monogenic, high heritability resistance traits, in cases where exposure of the population to the stressor would be costly, e.g. introgression of a monogenic resistance trait in fruit trees or cattle, where dealing with the pathogen during exposure is bothersome, or where it is difficult to apply the stressor. TB analyses would also be useful for analysis of marker-QTL linkages in the initial four to six generations of a selection program initiated from a cross between two inbred lines.

When an entire F-2 or BC population can be scored with respect to quantitative and marker traits, the MB analysis will generally be the method of choice, since it enables the same marker information to be used in the analysis of a large number of quantitative traits, and provides the maximum amount of information per individual tested. Even in this case, however, a TB analysis can be a useful alternative when the analysis is aimed at one quantitative trait and when measurement of the quantitative trait, including the cost of generating F-2 or BC individuals is considerably less costly than the marker determinations. Similar considerations would apply when many individuals are measured for the quantitative traits as part of routine collection of data for management or experimental studies.

TB analyses would be particularly useful for detecting pleiotropic effects of marker loci on quantitative traits in a segregating population, at or near linkage equilibrium (Beckmann and Soller 1986b; Gutwein 1976). In this case, one would screen a very large population to find the phenotypically extreme individuals, and score for marker allele frequencies in these phenotypically extreme tails. Under conditions of linkage equilibrium, a comparison of this sort will tend to detect pleiotropy rather than linkage.

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