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Marker-assisted selection in an outbred poultry breeding nucleus

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Abstract

The value of using a marker for a quantitative trait locus (QTL) affecting a sex-limited trait in an outbred poultry breeding nucleus was studied. Marker and QTL were in linkage equilibrium in the base population. The recombination rate between marker and QTL was 0·05. A closed nucleus with 9000 chickens per generation was deterministically simulated. The genetic model contained polygenes and a QTL linked to a marker. Genetic effects explained proportionately 0·3 of the phenotypic variance before selection. Under selection, polygenic variance reached an equilibrium and QTL variance decreased continuously over time. Cocks were selected in two steps. First the best cocks of each full-sib family were selected (within-family selection) while final selection took place after information on full-sibs was available. Hens were selected after they had completed production. The effect of using marker information in estimating breeding values was studied in an ongoing breeding programme. Transmission of marker alleles was always traceable. Cumulative response over five generations increased proportionately by 0·06 to 0·13 if a marker linked to a QTL that explained 0·2 of the genetic variance was used. Cumulative response increased up to 0·28 if the QTL explained 0·8 of the genetic variance. Additional response due to the use of a marker increased with increasing intensity of within-family selection of cocks, increased with increasing variance explained by the QTL and was higher if within-family selection of cocks was carried out after rather than before their sibs had complete records.

Keywords: *genetic markers, genetic models, poultry, selection responses.*

Introduction

In most livestock breeding schemes breeding values for quantitative traits are estimated using phenotypic information and additive genetic relationships among animals. The genetic model underlying the breeding value estimation assumes that an infinite number of genes each with an infinitely small effect influence the quantitative trait. However, an increasing number of genes or chromosome segments that explain a significant part of the variation in quantitative traits, are being identified. Use of this knowledge can improve current breeding value estimation procedures (Soller, 1994). Once a gene is located and the alleles of the gene identified, the effects of those alleles can be incorporated in breeding value estimation (Smith, 1967). If a marker is available that is linked to a locus explaining variation in a quantitative trait (i.e. a quantitative trait locus: QTL) marker-assisted breeding value estimation may be applied. Procedures for combining marker information and phenotypic information in selection index (Soller, 1978) or best linear unbiased prediction (Fernando and Grossman, 1989) have been described.

The use of markers can improve the selection response in a breeding programme (Soller, 1978; Soller and Beckmann, 1983; Smith and Simpson, 1986; Stam, 1986; Kashi, Hallerman and Soller, 1990; Dentine, 1992; Meuwissen and van Arendonk, 1992). Factors that influence the additional selection response include: (1) amount of variance explained by identified QTL(s); (2) distance between a marker and a QTL; (3) marker polymorphism; (4) the structure of the breeding programme; and (5) type of breeding goal trait (sex-limited or not). Dairy cattle breeding was the subject of the studies mentioned above. The structure of a poultry breeding population differs from the structure of a dairy cattle breeding population and therefore we cannot predict

from those dairy cattle breeding studies the value of marker-assisted selection (MAS) in poultry breeding. Most studies computed additional selection response for one round of selection starting from an unselected base generation. Meuwissen and van Arendonk (1992) computed equilibrium response assuming the variance accounted for by markers remained constant over generations. The latter assumption is unrealistic if a marker is linked to one or a few QTLs of large effect.

We studied the value of using a marker for a QTL in a poultry breeding nucleus. We used a genetic model in which each round of selection reduces the variance explained by a QTL. The genetic model was used in deterministic simulations to quantify the additional response due to MAS and the change of this additional response over time.

Methods

Breeding programme

A poultry breeding nucleus with non-overlapping generations is simulated. In a hierarchical mating scheme each sire is mated to several dams and several offspring are produced by each dam. Selection is for egg production, a sex-limited trait. Egg production is measured on all hens hatched. Each hen can be selected without a restriction on the number of full-sibs selected. Hens are selected after they have completed their first record. Selection of cocks differs among alternative breeding schemes. If no marker information is available then only the *max-c* first hatched cocks are candidates for selection, where *max-c* is the maximum number of cocks that may be selected from a full-sib family. This is random selection. With markers, this marker information is used to select *max-c* cocks from all available cocks in a full-sib family. This is called within-family selection. Marker-assisted within-family selection is either immediately after hatching (juvenile within-family selection) or after female sibs have complete records (adult within-family selection). In both cases all cocks are kept until the time of selection.

Deterministic simulation

Response per generation is computed as:

$$R = (R_w + R_c + R_h)/2 \qquad (1)$$

where R is the response per generation, R_w is the response to within-family selection of cocks, R_c is the response to final selection of cocks, and R_h is the response to selection of hens.

The deterministic simulation starts in generation zero, the base generation of unrelated animals. Each sire in the base generation has an estimated breeding value of zero. Breeding values for dams in the base generation are estimated using own performance. After five generations of selection, a marker is introduced. Introduction is not in generation zero to study the effect of introducing a marker in an ongoing breeding programme. One marker is introduced. Each animal in generation five and its parents are typed for this marker. Each parent is assumed to be heterozygous for the marker. Transmission of marker alleles can be traced without error. Let M1M2 be the marker genotype of a sire and M3M4 the marker genotype of a dam. The full-sib offspring are divided in four groups of equal size based on their marker genotype: M1M3, M1M4, M2M3 or M2M4.

Selection indices accounting for marker information are derived for cocks and hens. The selection index depends on the marker genotype of the candidate for selection. For each of the four possible marker genotypes a selection index is derived. The mean and variance of each index are computed. Equation (2) gives the response per generation allowing for the different selection indices:

$$R_t = \Bigg\{ \sum_{j=1}^{4} f_{wtj} \times (m_{wtj} - (\bar{m}_{wt} + i_{wtj} \times \sigma(\hat{A}_{wtj})) + \sum_{j=1}^{4} f_{ctj} \times (m_{ctj} - (\bar{m}_{ct} + i_{ctj} \times \sigma(\hat{A}_{ctj})) + \sum_{j=1}^{4} f_{htj} \times (m_{htj} - (\bar{m}_{ht} + i_{htj} \times \sigma(\hat{A}_{htj})) \Bigg\} / 2 \qquad (2)$$

where R_t is the response in generation t, f_{wtj} is the fraction selected of cocks with within-family selection index j in generation t, m_{wtj} is the mean genetic value before within-family selection of cocks with within-family selection index j in generation t, $\bar{m}_{wt}$ is the mean of all cocks before within-family selection in generation t, i_{wtj} is the selection intensity within the group of cocks with within-family selection index j in generation t, and $\sigma(\hat{A}_{wtj})$ is the standard deviation of within-family selection index j in generation t. The **Appendix** illustrates the use of (2) to compute within-family selection response.

Effect of selection on genetic (co)variances and (co)variances between information sources is accounted for after each selection step (Cochran, 1951). For hens there is one selection step in each generation. For cocks, (co)variances are corrected both after within-family selection and after final selection. Before each selection step, genetic effects are assumed to follow a multivariate normal distribution.

The effect of inbreeding on (co)variances is ignored. Derivation of selection index and computation of selection intensities will be described in later sections.

Genetic model

Genetic variance is due to additive gene action at one QTL and polygenes unlinked to the QTL. The breeding value of an animal is the effect of the paternal allele at the QTL plus the effect of the maternal allele at the QTL plus the effect of the polygenes. The model for the breeding value of animal i is :

$$a_i = v_i^p + v_i^m + u_i \quad (3)$$

where a_i is the breeding value of animal i, v_i^p is the effect of the paternal QTL allele, v_i^m is the effect of the maternal QTL allele, and u_i is the polygenic effect. Genetic effects are random and multivariate normally distributed. In the base generation before selection, the variance of a QTL allele is $\sigma^2(v^0)$, polygenic variance is $\sigma^2(u^0)$, genetic variance is $\sigma^2(a^0) = 2\sigma^2(v^0) + \sigma^2(u^0)$, and covariance between the effect of a QTL allele and the polygenic effect is zero.

A marker linked to the QTL is available. The relation between the allelic effects of the QTL of animal i and the allelic effects of the parents depends on marker information (Fernando and Grossman, 1989):

$$v_i^p = (1 - q_s)\, v_s^p + q_s v_s^m + \varepsilon(v_i^p) \quad (4)$$

$$v_i^m = (1 - q_d)\, v_d^p + q_d v_d^m + \varepsilon(v_i^m) \quad (5)$$

where s denotes the sire, d the dam, and $\varepsilon\,(v_i^p)$ is the part of v_i^p not explained by the regression on the parental allelic effects. The term $(1 - q_s)$ is the probability that the sire transmits its paternal QTL allele and q_s is the probability that the sire transmits its maternal QTL allele. Let r be the recombination rate between the marker and the QTL. The value of q_s is r if animal i inherits the paternal marker allele of the sire and q_s is $(1 - r)$ if animal i inherits the maternal marker allele of the sire.

For polygenic effects the following relation holds:

$$u_i = 0{\cdot}5u_s + 0{\cdot}5\, u_d + \varepsilon(u_i) \quad (6)$$

where $\varepsilon(u_i)$ is the part of u_i not explained by the regression on the parental polygenic effects.

Equations (4), (5) and (6) are used to compute the covariance between genetic effects of different animals. The covariance between the effect of a QTL allele in animal j and the effect of the paternal QTL allele in animal i is computed using the covariance between the QTL allele of animal j and the effects of the QTL alleles of the sire of animal i (Fernando and Grossman, 1989):

$$\sigma(v_j^p, v_i^p) = (1 - q_s)\, \sigma\,(v_j^p, v_s^p) + q_s\, \sigma(v_j^p, v_s^m) \quad (7)$$

where $\sigma(v_i^p, v_j^p)$ is the covariance between the paternal QTL allele of animal i and the paternal QTL allele of animal j. Equations similar to (7) were derived for the covariance between maternal QTL alleles or between a paternal and a maternal QTL allele. Fernando and Grossman (1989) describe a tabular method with repeated use of (7) to compute the covariance between any pair of QTL alleles. The covariance between the polygenic effect of animal j and the effect of the paternal QTL allele of animal i is:

$$\sigma(u_j, v_i^p) = (1 - q_s)\, \sigma(u_j, v_s^p) + q_s\, \sigma(u_j, v_s^m) \quad (8).$$

In the base generation before selection the covariance between polygenic effects and QTL allelic effects is zero. Selection will introduce a non-zero covariance between polygenic effects and allelic effects at the QTL in later generations.

In each generation the variance before selection of allelic effects at the QTL is computed. We assume that the expectations and variances of the QTL allelic effects in the selected group of sires and dams completely determine the variance of QTL alleles in the next generation. In the next generation the variance of a paternal allelic effect at the QTL is:

$$\sigma^2(v_i^p) = (1 - q_s)\, \sigma^2(v_s^p) + q_s\, \sigma^2(v_s^m) + (1 - q_s)\, q_s (E(v_s^p - v_s^m))^2 \quad (9)$$

where $\sigma^2(v_i^p)$ is the variance of the paternal QTL allele of animal i, $\sigma^2(v_s^p)$ is the variance after selection of the paternal QTL allele of the sire, $\sigma^2(v_s^m)$ is the variance after selection of the maternal QTL allele of the sire, $E(v_s^p)$ is the expectation after selection of the paternal QTL allele of the sire, and $E(v_s^m)$ is the expectation after selection of the maternal QTL allele of the sire.

The variance of polygenic effects before selection is:

$$\sigma^2(u_i) = 0{\cdot}25\, \sigma^2(u_s) + 0{\cdot}25\, \sigma^2(u_d) + 0{\cdot}5\, \sigma^2(u^0) \quad (10).$$

Selection index

Selection is for an index including observations on full-sibs, half-sibs, own performance for hens, and estimated breeding values of parents. Estimated breeding values of parents are based on sibs of the parents and information from earlier generations but not on information from offspring. The selection index is computed by regression on groups of

observations. The groups are defined such that some groups are absent in the conventional index without marker information and present in the marker-assisted selection index. For conventional selection (CS) the index is:

$$\hat{A}_c = b_{c1}(\overline{DP} - \overline{SP}) + b_{c2}\,\overline{SP} + b_{c3}(\hat{A}_s + \hat{A}_d) \qquad (11)$$

for cocks and:

$$\hat{A}_h = b_{h1}(\overline{DP} - \overline{SP}) + b_{h2}\,\overline{SP} + b_{h3}(\hat{A}_s + \hat{A}_d) + b_{h4}X_h \qquad (12)$$

for hens, where c denotes cock, h denotes hen, $\hat{A}$ is estimated breeding value, $\overline{DP}$ is the mean performance of all progeny of the dam, $\overline{SP}$ is the mean performance of all progeny of the sire, X_h is hen own performance, and bs are the regression coefficients.

The selection index is expanded to accommodate marker information. Regression on the difference in mean performance between groups of offspring that inherit alternative marker alleles from the parent is included as well as regression on estimated parental QTL effects:

$$\hat{A}^*_c = b^*_{c1}(\overline{DP} - \overline{SP}) + b^*_{c2}(\overline{SP}) + b^*_{c3}(\hat{A}^*_s + \hat{A}^*_d) + b^*_{c5}(\overline{DP}^p_d - \overline{DP}^m_d) + b_{c6}(\overline{SP}^p_s - \overline{SP}^m_s) + b^*_{c7}(\hat{v}^p_s - \hat{v}^m_s) + b^*_{c8}(\hat{v}^p_d - \hat{v}^m_d) \qquad (13)$$

for cocks and:

$$\hat{A}^*_h = b^*_{h1}(\overline{DP} - \overline{SP}) + b^*_{h2}\,\overline{SP} + b^*_{h3}(\hat{A}^*_s + \hat{A}^*_d) + b^*_{h4}X_h + b^*_{h5}(\overline{DP}^p_d - \overline{DP}^m_d) + b^*_{h6}(\overline{SP}^p_s - \overline{SP}^m_s) + b^*_{h7}(\hat{v}^p_s - \hat{v}^m_s) + b^*_{h8}(\hat{v}^p_d - \hat{v}^m_d) \qquad (14)$$

for hens, where $\hat{A}^*$ is the estimated breeding value if marker information is used, $\overline{DP}^p_d$ is the average performance of progeny of the dam that inherit the paternal marker allele from the dam, $\overline{DP}^m_d$ is the average performance of progeny of the dam that inherit the maternal marker allele from the dam, $\overline{SP}^p_s$ is the average performance of progeny of the sire that inherit the paternal marker allele from the sire, $\overline{SP}^m_s$ is the average performance of progeny of the sire that inherit the maternal marker allele from the sire, $\hat{v}$ is the estimated effect of a QTL allele.

A within-family selection index is defined that estimates the deviation of the breeding value of the selection candidate from the full-sib family mean. The juvenile within-family selection index is:

$$WF\text{–}ju = b_{j1}(\hat{v}^p_s - \hat{v}^m_s) + b_{j2}(\hat{v}^p_d - \hat{v}^m_d) \qquad (15)$$

and the adult within-family selection index is:

$$WF\text{–ad} = b_{a1}(\overline{DP}^p_d - \overline{DP}^m_d) + b_{a2}(\overline{SP}^p_s - \overline{SP}^m_s) + b_{a3}(\hat{v}^p_s - \hat{v}^m_s) + b_{a4}(\hat{v}^p_d - \hat{v}^m_d) \qquad (16).$$

The selection indices do not allow for grandparental origin of parental marker alleles, i.e. animal A with a sire that inherited a paternal marker allele from the grandsire, is not distinguished from animal B with a sire that inherited a maternal marker allele from the grandsire. Therefore, for sire and dam effects (co)variances like $\sigma^2(v^p_s)$ are used that are independent from marker information. To compute unconditional (co)variances the general formula (Biswas, 1991): $\text{cov}(X,Y) = (E(\text{cov}\ (X,\ Y \mid Z)) + \text{cov}\ (E(X \mid Z), E\ (Y \mid Z))$ is used.

Computation of selection intensities

For each selection step we consider four indices, one for each marker genotype. Each index has an expectation and a variance. Due to differences in expectations and variances of indices, the proportions selected per index differ. For the final male selection step and the female selection step, the algorithm described by Ducrocq and Quaas (1988) has been used to compute the selection fractions and selection intensities for the four indices. These selection intensities are then corrected for finite population size (Burrows, 1972).

For within-family selection of cocks each index has only one realization within a family. No deterministic method is available to compute selection intensities for this case. Therefore, a simple stochastic simulation was used. For each index one random realization was simulated using the expectation and variance of the index. This realization was assigned to a quarter of the cocks in the family. Then, the cocks with the best index were assumed to be selected. The marker genotype of the selected cocks and the index value were recorded. For each generation this was repeated 10 000 times. The proportion selected per index, the selection intensity per index, and the reduction of variance per index were computed from simulation results.

Simulated schemes

In the standard scheme 50 sires were used per generation. Each sire was mated to six dams and each dam produced 30 offspring, 15 cocks and 15 hens. *Max-c* was 6. In the unselected and unrelated base generation, heritability was 0·3 and the proportion of the genetic variance due to the QTL was 0·2. The recombination rate between marker and QTL was 0·05. Population structure varied leaving genetic parameters constant. Number of sires (N_s)

and number of offspring per sire (180) were constant. For numbers of dams per sire (N_d) the values 3, 6 and 9 were used. Number of offspring per dam (N_o) was $180/N_d$. For *max-c* the values 3, 6 and 9 were used. Schemes representing all nine combinations of N_d and *max-c* were simulated. In other alternative schemes, genetic parameters varied leaving population structure constant. For proportion of genetic variance due to the QTL the values 0, 0·1, 0·2, 0·4, 0·6, and 0·8 were used and for heritabilities the values 0·1, 0·3 and 0·5. Schemes representing all 18 combinations of proportion of genetic variance due to the QTL and heritability were simulated.

Results

Standard breeding scheme

Table 1 gives the responses to within-family selection and total response per generation for the standard breeding scheme. The response per generation was highest in generation zero. After generation zero, response decreased due to reduced genetic variances (Table 2). Response did not reach an equilibrium because QTL variance decreased continuously (Table 2). Response increased after introduction of a marker in generation 5. QTL response increased from 0·110 in generation 4 to 0·178 in generation 5 while polygenic response decreased from 0·460 in generation 4 to 0·445 in generation 5. The within-family response in generation 5 was 0·034 which is 0·19 times the QTL response. After generation 5 within-family response first increased and then gradually decreased, whereas QTL response due to final male selection and female selection constantly decreased. In generation 20 the within-family response was 0·28 times the QTL response. Polygenic response increased after generation 5 both for CS and for MAS. Over generations polygenic response increased more for MAS than for CS. QTL variance reduced more when MAS was applied. Therefore, the proportion of genetic variance due to polygenes increased more for MAS than for CS. In absolute values polygenic variance hardly differed between MAS and CS.

Table 1 *QTL-, polygenic- and total- response per generation for standard breeding scheme with conventional selection (CS) or marker-assisted selection (MAS)*

	QTL response			Polygenic response		Total response	
t†	CS	MAS‡		CS	MAS	CS	MAS
0	0·155			0·621		0·776	
4	0·110			0·460		0·570	
5	0·108	0·178	(0·034)	0·461	0·445	0·569	0·622
10	0·100	0·166	(0·042)	0·464	0·450	0·564	0·616
15	0·093	0·141	(0·038)	0·467	0·458	0·560	0·600
20	0·087	0·122	(0·034)	0·469	0·465	0·556	0·587

† *t* is the generation.
‡ Between brackets is the QTL response to within-family selection of cocks.

Table 2 *QTL variance* (σ^2(q)‡), *polygenic variance* (σ^2(u)) *and genetic variance* (σ^2(a)) *before selection of different genetic effects for standard breeding scheme with conventional selection (CS) or marker-assisted selection (MAS)*

	σ^2 (*q*)		σ^2 (*u*)		σ^2 (*a*)	
t†	CS	MAS	CS	MAS	CS	MAS
0	0·060		0·240		0·300	
4	0·055		0·198		0·232	
5	0·054	0·054	0·198	0·198	0·231	0·231
10	0·050	0·046	0·197	0·200	0·228	0·223
15	0·046	0·038	0·197	0·199	0·225	0·217
20	0·043	0·033	0·196	0·198	0·223	0·213

† *t* is the generation.
‡ $\sigma^2(q)$ is the variance of quantitative trait *locus* i.e. $\sigma^2(v^p + v^m)$.

Figure 1 gives the QTL response per generation relative to the QTL response in generation zero. Further, the polygenic response per generation relative to polygenic response in generation zero is given. Polygenic response was fairly constant after two generations with a slight decrease after the

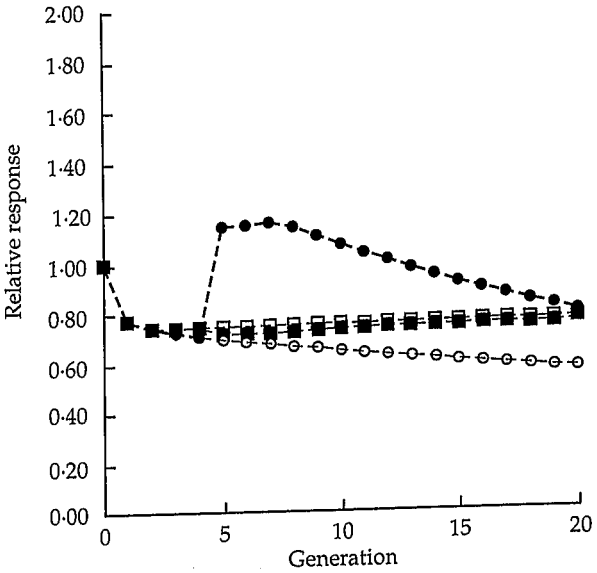

Figure 1 QTL response to conventional selection (○), polygenic response to conventional selection (□), QTL response to marker-assisted selection (●), and polygenic response to marker-assisted selection (■) in generations 0 to 20 for standard breeding scheme. All responses are relative to corresponding response in generation zero.

introduction of marker information. QTL response to conventional selection decreased constantly. QTL response increased sharply after introduction of a marker in generation 5. After generation 5 the QTL response to MAS decreased at a higher rate than for conventional selection. As a result, the difference in QTL response between MAS and CS slightly decreased over generations.

Figure 2 gives the standardized QTL response and standardized polygenic response. In each generation, QTL response is divided by the covariance between QTL and breeding value ($\sigma(v^p_i + v^m_i, a_i)$) before selection in that generation. Polygenic response is divided by the covariance beween polygenic effect and breeding value ($\sigma(u_i, a_i)$). Standardization was used to correct for the effect of variance reduction. Standardized polygenic response to MAS, standardized polygenic response to CS, and standardized QTL response to CS can hardly be distinguished. Standardized QTL response to MAS differed clearly from the other three. Standardized QTL response increased sharply after introduction of marker information in generation 5. After generation 5 standardized QTL response to MAS increased further while the other standardized responses remained constant. The results for CS in Figure 2 show that reduced variance influenced polygenic response and QTL response similarly although selection influences polygenic variance differently than QTL variance. Figure 2 further shows that standardized QTL response was constant without markers, but increased over generations when a marker was used. The decrease in absolute QTL response over generations (Figure 1) shows that reduced QTL variance had a larger effect than increased standardized QTL response.

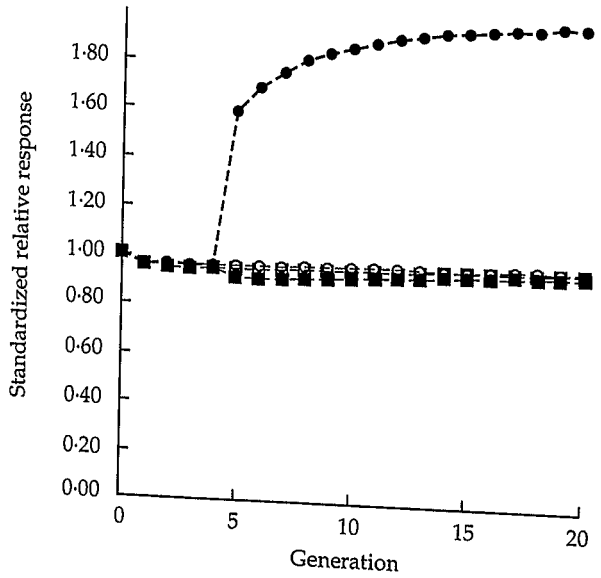

Figure 2 Standardized QTL response to conventional selection (○), standardized polygenic response to conventional selection (□), standardized QTL response to marker-assisted selection (●), and standardized polygenic response to marker-assisted selection (■) in generations 0 to 20 for standard breeding scheme. All standardized responses are relative to standardized response in generation zero.

Table 3 *Response per generation and cumulative response for conventional selection for various breeding schemes*†

N_d	N_o	*max-c*	Generation 5	Generation 9	Cumulative over generations 5 to 9
3	60	3	0·553	0·548	2·751
		6	0·589	0·584	2·935
		9	0·610	0·604	3·034
6	30	3	0·536	0·531	2·668
		6	0·569	0·565	2·836
		9	0·588	0·584	2·928
9	20	3	0·523	0·520	2·608
		6	0·555	0·553	2·769
		9	0·573	0·571	2·859

† Varied are number of dams per sire (N_d), number of full-sib offspring per dam (N_o) and the maximum number of cocks selected per full-sib family (*max-c*).

Alternative schemes

Table 3 gives the response in generations 5 and 9, and cumulative response over generations 5 to 9 to conventional selection for various breeding schemes. Number of dams per sire (N_d), number of offspring per dam (N_o) and *max-c* varied between schemes. Number of sires (N_s) and number of offspring per sire ($N_d \times N_o$) were constant. Response per generation increased with increasing *max-c* and with decreasing N_d. The reason for this is that male final selection intensity increased with increasing *max-c* and female selection intensity increased with decreasing N_d.

Table 4 gives the additional response due to markers relative to response to CS. Cumulative additional response was proportionately 0·06 to 0·13 of the cumulative conventional response. Additional response was higher for schemes with adult within-family selection than for schemes with juvenile within-family selection. This was especially true in generation 5 where additional response varied from proportionately 0·046 to 0·05 for juvenile schemes and from 0·057 to 0·122 for adult schemes. In generation 5 within-family response is zero for

Table 4 *Additional response due to marker-assisted selection as a proportion of conventional response for various breeding schemes*†

				Generation 5		Generation 9		Cumulative over 5 to 9	
N_d	N_o	*max-c*	i_{rw}‡	ju§	ad¶	ju	ad	ju	ad
3	60	3	1·036	0·047	0·122	0·091	0·101	0·082	0·111
		6	1·039	0·049	0·116	0·092	0·101	0·081	0·108
		9	0·916	0·050	0·106	0·084	0·091	0·075	0·098
6	30	3	1·048	0·046	0·116	0·111	0·126	0·092	0·124
		6	0·774	0·048	0·093	0·091	0·096	0·078	0·097
		9	0·518	0·049	0·076	0·073	0·073	0·066	0·075
9	20	3	0·936	0·047	0·108	0·121	0·134	0·097	0·127
		6	0·523	0·049	0·077	0·087	0·087	0·075	0·085
		9	0·121	0·050	0·057	0·065	0·065	0·060	0·062

† Varied are number of dams per sire (N_d), number of full-sib offspring per dam (N_o) and the maximum number of cocks selected per full-sib family (*max-c*).
‡ i_{rw} is the realized within-family selection intensity, computed as the within-family response divided by the standard deviation of the within-family index, averaged over generations 5 to 9. The given values are for adult within-family selection. Realized intensity of juvenile within-family selection, computed over generations 6 to 9 because juvenile within-family selection response is zero in generation 5, was between 0·1% and 1·8% higher than realized intensity of adult within-family selection.
§ ju is the additional response as proportion of conventional response for schemes with juvenile within-family selection.
¶ ad is the additional response as proportion of conventional response for schemes with adult within-family selection.

juvenile schemes because there is no information to estimate within-family deviations. For adult schemes in generation 5, sib information is available to estimate within-family deviations. Cumulative over generations 5 to 9, additional proportional response in juvenile schemes varied from 0·06 for N_o at 20 and *max-c* at 9 to 0·097 for N_o at 20 and *max-c* at 3. Cumulative additional response in adult schemes varied from 0·062 for N_o at 20 and *max-c* at 9 to 0·127 for N_o at 20 and *max-c* at 3. Additonal response increased with decreasing *max-c*. With decreasing *max-c*, the within-family selection intensity increased and therefore response to within-family selection increased. Additional response also increased with decreasing N_d at a given proportion of male offspring selected from within a family, i.e. additional response is higher with N_d at 6 and 3 out of 30 selected, than with N_d at 3 and 6 out of 60 selected. With increasing N_d the differences in precision of the effects of paternally and maternally derived QTL alleles increased. Differences between mean values of paternal and maternal alleles after selection increased with increasing N_d. Different expectations for maternal and paternal QTL alleles result in different expectations for the four selection indices. These differences can be exploited in selection.

Figure 3 shows how the proportion of genetic variance due to the QTL and heritability affect additional response. If the proportion of the genetic variance due to the QTL was 0·10 then additional response was highest for a heritability of 0·5 and lowest for a heritability of 0·1. If the proportion of the genetic variance due to the QTL was 0·20 then additional response hardly changed by changing heritability. For proportions due to QTL higher than 0·20, additional response was highest for a heritability of 0·1 and lowest for a heritability of 0·5. For a proportion due to the QTL of 0·20, as in the standard scheme, additional proportional response

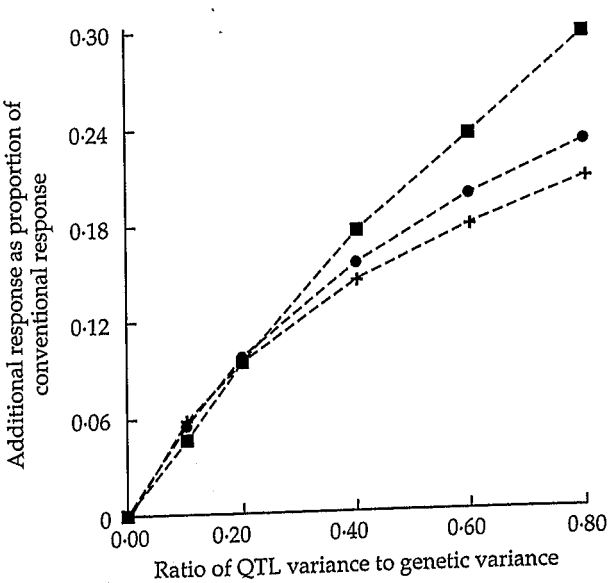

Figure 3 Effect of proportion of genetic variance due to QTL on additional response for heritabilities at 0·1 (■), 0·3 (●). and 0·5 (+).

was 0·095 for a heritability of 0·1, 0·097 for a heritability of 0·3, and 0·095 for a heritability of 0·5. For a proportion due to the QTL of 0·80, additional proportional response was 0·278 for a heritability of 0·1, 0·229 for a heritability of 0·3, and 0·206 for a heritability of 0·5.

Discussion

Use of a marker linked to a QTL that explained a proportion of 0·2 of the genetic variance of a sex-limited trait increased response proportionately with 0·06 to 0·127. Increasing the proportion of the genetic variance explained by the QTL to 0·8 resulted in increases in proportional response up to 0·278. In other studies MAS resulted in 0·20 to 0·30 (Kashi *et al.*, 1990), 0·10 and 0·25 (Meuwissen and van Arendonk, 1992) and 0·40 (Stam, 1986) proportional increases in response. Stam (1986) studied sib selection of young bulls in a dairy cattle breeding scheme. The 0·40 proportional increase was realized assuming that the true breeding value of a bull's sire was known with using markers and all genetic variance was due to one locus for which segregation could be observed. Kashi *et al.* (1990) and Meuwissen and van Arendonk (1992) looked at the situation when the whole genome was covered with markers that were used to find associations in large groups of offspring of elite sires. Kashi *et al.* (1990) selected young bulls before entering the progeny test based on the marker alleles they inherited from their grandsires. In the work of Meuwissen and van Arendonk (1992) there was only one selection step. Marker associations found in grandsires were used to estimate within-family deviations either in a progeny testing scheme or in a nucleus breeding scheme.

There are important differences between our study and the last two studies mentioned above. The within-family selection of cocks in our study is similar to MAS of young bulls in Kashi *et al.* (1990). The final selection steps of cocks and hens in our study are similar to the use of markers in a nucleus herd as in Meuwissen and van Arendonk (1992). So, we combined two methods of obtaining additional response but our additional responses are lower than either those of Kashi *et al.* (1990) or those of Meuwissen and van Arendonk (1992). The reasons for this are: (1) we computed cumulative response over five generations using a model in which QTL variance and consequently QTL response declines over generations, while Kashi *et al.* (1990) computed response for one generation and Meuwissen and van Arendonk (1992) computed equilibrium response assuming no decline in QTL response; (2) we considered one QTL explaining only part of the genetic variance and not the whole genome; (3) in dairy cattle breeding programmes more information is available to estimate marker allelic effects. In a poultry breeding programme only information from within the nucleus can be used for breeding value estimation, whereas in the dairy cattle breeding schemes marker allelic effects in elite sires are estimated using many offspring from outside the nucleus. Of course, the structure of a poultry breeding programme can be changed to estimate marker allelic effects more accurately. Because of such a change the polygenic part of the breeding value will, however, be estimated more accurately too. Consequently, additional response will not increase proportionally.

Additional response increased with increasing QTL variance. For proportions of genetic variance due to the QTL of above 0·20, additional response increased with decreasing heritability. For proportions of genetic variance due to the QTL under 0·20, additional response decreased with decreasing heritability. This observed interaction is not fully understood.

We assumed that the transmission of all marker alleles is always traceable. For microsatellite markers, a highly polymorphic class of markers, on average a heterozygosity of 0·28 was observed in commercial layer lines (Groen, Crooijmans, van Kampen, van der Beek, van der Poel and Groenen, 1994). Allele frequencies were estimated for several microsatellite markers and heterozygosity was estimated assuming Hardy Weinberg equilibrium (Groen *et al.*, 1994). Given this level of polymorphism, marker transmission will often be untraceable which will have a negative influence on the benefits of MAS (Kashi *et al.*, 1990). The use of several closely linked markers largely solves the problem of untraceable marker transmission (Kashi *et al.*, 1990). This, however, will generate additional costs of typing.

Inbreeding was ignored in this study. Without selection we can predict from the number of sires and dams used per generation that inbreeding would increase at a proportional rate of 0·003 per generation. At this rate, inbreeding will hardly affect response. With selection, however, inbreeding will increase more rapidly since sibs will be co-selected, especially males. This will especially lower the level of response of schemes with a high *max-c* and high N_o. The exact impact of inbreeding on QTL response is hard to predict.

Responses were given per generation. The effect of generation interval was not included. For all schemes, either with or without the use of markers,

final selection of males and females was after the females in a generation had completed their first record. The use of markers did not alter the generation interval and therefore additional response expressed as proportion of response to conventional selection was independent of generation interval. Comparisons over schemes were based on additional response. So, although generation interval might differ between schemes, comparisons were not affected by generation interval.

The genetic model in this study assumed a QTL with allelic effects that follow a normal distribution. Selection reduced the variance of the allelic effects. Recombination during the forming of new gametes did not counterbalance the reduction of QTL variance. In each round of selection, therefore, QTL variance was further reduced whereas for polygenic variance, recombination and selection reached an equilibrium. The proportion of the genetic variance due to the QTL, therefore, decreased over generations and consequently also the additional response due to MAS. Polygenic response, after an initial decrease due to a build up of linkage disequilibrium after selection in generation zero, gradually increased over time. This can be explained as follows: QTL variance decreases and therefore also negative covariance between polygenic and QTL effects. Therefore, the covariance between additive genetic effects and polygenic effects increases and also the polygenic response. Polygenic response was lower with MAS than with CS. This is due to the negative covariance between QTL effects and polygenic effects. QTL response is higher with MAS than with CS and consequently also the correlated negative effect on polygenic response is higher with MAS than with CS.

We believe our genetic model is more realistic than a model that assumes a constant QTL response over generations. Our model, however, sets no limit to the cumulative QTL response. This is unrealistic for a single locus with a finite number of allelic effects in the base generation. A solution could be the introduction of a 'best allele model' in which the population mean for the QTL cannot increase above the value of an animal homozygous for the best QTL allele in the base generation. A heuristic approach might be to let the QTL variance after selection depend on the cumulative QTL response. Alternatively, the single locus model can be interpreted as a model for a cluster of many closely linked loci. For a given QTL variance in the base generation long-term response will increase with increasing number of underlying genes and our model will become more realistic. The same argument applies for a situation with several independent marked QTLs.

We studied the additional respnse due to MAS for a poultry breeding nucleus assuming favourable conditions like a sex-limited trait, a restriction on the number of cocks selected per full-sib family and traceable marker alleles. For a commercial breeder increased response should lead to an improved market share or a higher price for its products. The costs are in collecting blood, isolating DNA and typing for marker loci. With the ongoing development of marker technology it is hard to quantify future costs of MAS. Predicting effects of additional response on market share is harder and will depend on the current position and strategies used by competitors. Given its position, the commercial poultry breeder can compare the costs and benefits of marker-assisted selection. Results of this study can help in this decision process and in implementing the new technology efficiently.

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Appendix

Here we show how to compute the within-family selection response in generation 10 of the standard scheme. From equation (2), the contribution to selection response of within-family selection is:

$$0{\cdot}5 \sum_{j=1}^{4} f_{wtj} \times (m_{wtj} - \bar{m}_{wt} + i_{wtj} \times \sigma(\hat{A}_{wtj}))$$

$$= 0{\cdot}5 \left(\sum_{j=1}^{4} f_{wtj} \times (m_{wtj} + i_{wtj} \times \sigma(\hat{A}_{wtj})) - \sum_{j=1}^{4} 0{\cdot}25 \times m_{wtj}\right) \quad \text{(A1)}$$

where f_{wtj} is the fraction selected of cocks with within-family selection index j in generation t, m_{wtj} is the mean genetic value before within-family selection of cocks with within-family selection index j in generation t, $\bar{m}_{wt}$ is the mean of all cocks before within-family selection in generation t, i_{wtj} is the selection intensity within the group of cocks with within-family selection index j in generation t, and $\sigma(\hat{A}_{wtj})$ is the standard deviation of within-family selection index j in generation t. The group of offspring that inherit two paternal marker alleles have index 1, the group that inherit a paternal allele from the sire and a maternal from the dam have index 2, the group that inherit a maternal allele from the sire and a paternal from the dam have index 3, and offspring that inherit two maternal marker alleles have index 4. Before within-family selection the four groups are of equal size.

The components required to compute within-family selection response are given in Table A1. Before selection, offspring inheriting a paternal marker allele from the sire are on average better than offspring inheriting a maternal marker allele from the sire. For a given sire allele, animals inheriting a paternal allele from the dam are better than animals inheriting a maternal one. As a result, after selection animals with two paternal alleles are most frequent, and animals with two maternal alleles are least frequent. This means that groups with lowest mean were most intensely selected. Equation (A1) shows that the within-family selection response can be computed from group means and fractions before and after selection as: 0·5 × (0·397 × 6·303 + 0·262 × 6·278 + 0·221 × 6·278 + 0·120 × 6·264 − 0·25 × (6·262 + 6·211 + 6·194 + 6·142)) = 0·042, which is the within-family response as also given in Table 1 for generation 10.

Table A1 *Elements required to compute the within-family selection response to marker-assisted selection in the standard scheme*

Index	Fraction before selection	Mean before selection	s.d. of index	Selection intensity	Fraction after selection	Mean after selection
1	0·250	6·261	0·096	0·438	0·397	6·303
2	0·250	6·211	0·098	0·705	0·262	6·278
3	0·250	6·194	0·102	0·810	0·221	6·278
4	0·250	6·143	0·104	1·135	0·120	6·264