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# Using genetic markers for disease resistance to improve production under constant infection pressure[1]

**E. H. van der Waaij*†[2], P. Bijma*, S. C. Bishop†, and J. A. M. van Arendonk***

*Animal Breeding and Genetics Group, Wageningen Institute of Animal Sciences, 6700 AH, Wageningen, The Netherlands and †Roslin Institute (Edinburgh), Roslin, Midlothian EH25 9PS, United Kingdom

**ABSTRACT:** Animals will show reduced production when exposed to a constant infection pressure unless they are fully resistant, the size of the reduction depending on the degree of resistance and the severity of infection. In this article, the use of QTL for disease resistance for improving productivity under constant infection pressure is investigated using stochastic simulation. A previously published model was used with two thresholds for resistance: a threshold below which production is not possible and a threshold above which production is not affected by the infection. Between thresholds, observed production under constant infection is a multiplicative function of underlying potential production and level of resistance. Some simplifications of reality were adopted in the model, such as no genetic correlation between potential production and resistance, the absence of influence of lack of resistance on reproductive capacity, and the availability of phenotypes in both sexes. Marker-assisted selection was incorporated by assuming a proportion of the genetic variance to be explained by the QTL, which thus is defined as a continuous trait. Phenotypes were available for production, not for resistance. The infection pressure may vary across time. Results were compared to mass selection on production under constant as well as intermittent infection pressure, where the infection pressure varied between but not within years. Selection started in a population with a very poor level of resistance. Incorporation of QTL information is valuable (i.e., the increase in observed production relative to mass selection) when a large proportion of the additive genetic variance is explained by the QTL (50% genetic variance explained) and when the heritability for resistance is low ($h^2_R = 0.1$). Under constant infection pressure, incorporating QTL information does not increase selection responses in observed production when the QTL effect explains less than 25% of the genetic variance. Under intermittent selection pressure, the use of QTL information gives a slightly greater increase in observed production in early generations, relative to mass selection on observed production, but still only when the QTL effect is large or the heritability for resistance is low. The additional advantage of incorporating QTL information is that use of (preventive) medical treatment is possible, or animals may be evaluated in uninfected environments.

Key Words: Disease Resistance, Genetics, Production, Quantitative Trait Loci, Selection, Stochastic Models

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## Introduction

Animals that are not fully resistant to a certain disease may show a decreased production when infected. A high infection pressure combined with a low level of resistance may cause production to drop to, or even below (in case of growth), zero. When the level of resistance is high, infection may have little or no influence on performance. Van der Waaij et al. (2000) presented a model describing the relationship between production under constant infection pressure and level of resistance. Their results suggest that selection for production under constant infection pressure results in an increase in potential production (the production that would have been achieved in the absence of infection), as well as in resistance. Trypanosomosis is an example of an important disease with constant infection pressure. Trypanotolerant local cattle breeds do exist, but both their resistance and production may be further improved.

A disadvantage of the model presented by Van der Waaij et al. (2000) is that exposure to the pathogen is required in order to get phenotypic observations for observed production. An alternative option would be to

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[2]Correspondence: P.O. Box 338 (phone: +31-317-482335; fax: +31-317-483929; E-mail: Liesbeth.vanderwaaij@alg.vf.wag-ur.nl).

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keep the animals in an uninfected environment, or under medication, and combine potential production with QTL for disease resistance, to predict production under constant infection pressure. Also, in Van der Waaij et al. (2000) it was assumed that infection pressure was constant. In reality, infection pressure may vary across time, resulting in intermittent (indirect) selection pressure on resistance when mass selection on observed production is applied. The use of QTL would enable selection pressure on resistance, irrespective of the presence of infection pressure.

The objective of this article is to investigate the use of resistance QTL for improving productivity under constant and intermittent infection pressure, avoiding exposing the animals to infection, where infection pressure is assumed constant within a season but different between seasons.

## Materials and Methods

### *Model*

The model of Van der Waaij et al. (2000) was used to describe the relationship between level of disease resistance (**R**) and observed production (**Po**) under infection pressure. In that model, the level of production that would have been achieved if the animal were completely resistant is denoted as production potential (**Pp**). Under infection pressure, the level of resistance of an animal to the infection affects observed production, so that observed production is a function of both production potential and resistance:

$$Po = f(R) \times Pp, \quad [1]$$

where f(R) is a function of resistance, which describes the effect of resistance on observed production. Van der Waaij et al. (2000) distinguished three categories of resistance, which are separated by thresholds. In the first category, animals are fully susceptible when their level of resistance is below the lower threshold (L), in which case production is no longer possible (Po = 0). In the second, animals are fully resistant when their level of resistance is above the upper threshold (U), in which case observed production equals production potential (Po = Pp). In the third category, animals between both thresholds are partly resistant and their observed production will be lower than their production potential, the size of the decrease depending linearly on the level of resistance. Thus, the effect of resistance on observed production is summarized by the following equations:

$$\begin{aligned} &f(R) = 0 \text{ for } R < L \\ &f(R) = (R - L)/(U - L) \text{ for } L < R < U \\ &f(R) = 1 \text{ for } R > U \end{aligned} \quad [2]$$

The thresholds were assumed to be fixed and their values depend on the type of infection and other environmental factors. It is assumed that resistance and production potential are normally distributed, that there is no correlation between production potential and resistance, and that values for resistance are not negative.

### *Selection*

Two selection strategies were considered. Selection was either based on the phenotype for observed production under infected circumstances or on a combination of QTL for disease resistance and phenotypic information on production potential under uninfected circumstances.

*Mass Selection Under Constant Infection.* Animals were ranked according to their phenotype for observed production under infected circumstances, after which truncation selection was applied. When animals were treated with medication, it was assumed that this treatment took place after observed production was recorded. When the number of animals with an observation for observed production is smaller than the number to be selected, additional animals were taken randomly from the group of animals with resistance below the lower threshold. Results of mass selection under constant infection pressure will be used as point of reference, against which results obtained using other selection criteria or intermittent infection pressure (described below) will be evaluated.

*QTL Selection.* In the absence of infection, phenotypic information on observed production is not available. In this situation, therefore, selection was based on an estimated breeding value for observed production, which was estimated using QTL information on resistance and phenotypic information on production potential. It was assumed that a number of QTL for resistance had been identified, which explain a fraction $p_m$ of the total additive genetic variance. The total QTL effect was assumed to be approximately normally distributed, with mean $\mu_{QTL}$ and a heritability of $h^2_{QTL} = 1.0$, because the QTL were supposed to be known without error. The proportion of variance explained by QTL remained constant over time (i.e., it was assumed that fixation of QTL due to selection was completely compensated for by identification of new QTL during the experiment).

In the strict sense, the estimated breeding value of an individual is defined as "twice the phenotypic performance of its offspring measured as a deviation from the population mean." In the usual mixed linear models, this definition is equivalent to the additive genetic merit of the individual itself, measured as a deviation from the population mean. In the present nonlinear model, however, expected offspring performance does not only depend on genetic merit of the parent, but also on the variance of the offspring performance around its mean. For example, when the mid-parent value for resistance is just above the upper threshold, phenotypic resistance of the offspring may still be below the upper threshold due to Mendelian sampling and environmental vari-

ance in resistance, which reduces observed production of the offspring. Thus, the estimated breeding value for observed production cannot simply be based on estimated genetic merit of parents, but the expected observed production of offspring need to be predicted. Because the breeding goal is to improve observed production under infection, offspring performance will be predicted for infected circumstances.

Observed production of an offspring was predicted from the mean of its parents and the variance of the offspring performance around this mean. Given the estimated breeding value for resistance of the parent, the phenotypic resistance of an offspring is normally distributed with mean $\frac{1}{2}ebv_p + \frac{1}{2}\overline{ebv_m}$ and variance $\sigma^2_{p_R} - \frac{1}{4}p_m\sigma^2_{A_R}$; $R_o \sim N(\frac{1}{2}ebv_p + \frac{1}{2}\overline{ebv_m}, \sigma^2_{p_R} - \frac{1}{4}p_m\sigma^2_{A_R})$, where $ebv_p$ is the estimated breeding value for resistance of the parent and $\overline{ebv_m}$ is the mate average. The term $\sigma^2_{P_R} - \frac{1}{4}p_m\sigma^2_{A_R}$ represents the phenotypic variance for resistance in the offspring given the parent (i.e., selection of the parent based on QTL for resistance explains an amount of $\frac{1}{4}p_m\sigma^2_{A_R}$ of the phenotypic variance of the offspring; note that the squared correlation between QTL-effect and breeding value for resistance equals $p_m$).

Depending on the mean and variance of $R_o$, a proportion $p_L$ of the offspring will have values for $R_o$ below the lower threshold, a proportion $p_U$ will have values above the upper threshold, and a proportion $p_B$ will have values between both thresholds. These proportions were determined as

$$p_L = \Phi\left(\frac{L - \frac{1}{2}ebv_p - \frac{1}{2}\overline{ebv_m}}{\sqrt{\sigma^2_{p_R} - \frac{1}{4}\rho^2\sigma^2_{A_R}}}\right),$$

$$p_U = 1 - \Phi\left(\frac{U - \frac{1}{2}ebv_p - \frac{1}{2}\overline{ebv_m}}{\sqrt{\sigma^2_{P_R} - \frac{1}{4}\rho^2\sigma^2_{A_R}}}\right),$$

and $p_B = 1 - p_u - p_L$, where $\Phi$ is the lower tail proportion of the standardized normal distribution. Potentially, one or two of the fractions $p_L$, $p_B$, or $p_U$ can be zero. Given the distribution of resistance in the offspring, observed offspring production was predicted by weighting observed production in each part of the distribution of $R_o$ by the appropriate proportion. Because Po = 0 for R < L, and Po = Pp for R > U, expected offspring production equals the following:

$$SC_{Po} = P_B \times Po_B + p_U \times Pp, \quad [3]$$

where $Po_B = [(\mu_{R_M} - L)/(U - L)] \times Pp_o$, which is the expected observed production for offspring with L < R < U, and $Pp_o = \frac{1}{2}\,Pp_{sire} + \frac{1}{2}\,Pp_{mate}$, which is the expected potential production of the offspring. Next, $\mu_{R_B}$, the expected phenotypic resistance of offspring with L < R < U, was calculated from $\mu_{R_B} = (\mu_{R_o} - p_U \times \mu_{R_U} - p_L \times \mu_{R_L})/p_B$, where $\mu_{R_U} = \mu_{R_o} + i_u\sigma_{P_{Ro}}$ is the expected phenotypic resistance of offspring with R > U and $\mu_{R_L} = \mu_{R_o} - i_L\sigma_{P_{Ro}}$ for offspring with R < L, and $i_L$ ($i_U$) is the "selection intensity" corresponding to $p_L$ ($p_U$).

Animals were ranked and selected by truncation according to their $SC_{po}$. In the remainder of this paper, predicted observed production of the offspring ($SC_{Po}$) will be referred to as "predicted production."

### *Environment: Infectious vs Noninfectious*

The model of Van der Waaij et al. (2000) was developed assuming constant infection pressure, which in reality often will not be the case. It is possible that, for example, even though infection pressure often is present, during performance recording the infection pressure is absent and observed production actually has become equal to production potential. So, during some generations selection may occur under infection pressure, whereas during other generations the infection pressure at the time of selection is absent. Mass selection on observed production in the absence of infection pressure will result in selection on production potential, neglecting resistance. Selection on predicted production puts selection pressure directly on production potential and indirectly on resistance via genetic marker information, independent of whether or not there is infection pressure.

In this paper, three schemes with intermittent infection pressure were compared: one generation with infection pressure followed by one generation without (1-1), three generations with infection followed by one generation without (3-1), and three generations with infection pressure followed by three generations without (3-3).

### *Stochastic Implementation*

A population was stochastically simulated (200 replicates), with both resistance and production potential modeled as heritable traits. Initial genotypes for production potential and resistance were randomly sampled from independent normal distributions with means ($\mu_{Pp}$ and $\mu_R$ and additive genetic variances $\sigma^2_{APp}$ and $\sigma^2_{AR}$. Environmental effects were randomly drawn from independent normal distributions with mean zero and variance $\sigma^2_{EPp}$ and $\sigma^2_{ER}$. Heritabilities for production potential ($h^2_{Pp}$) and resistance ($h^2_R$) in the base population were $h^2 = \sigma^2_A/\sigma^2_P$, where $\sigma^2_A$ and $\sigma^2_P$ represent the respective additive genetic and phenotypic variance ($\sigma^2_P = \sigma^2_A + \sigma^2_E$). Heritabilities were varied by varying $\sigma^2_A$. Phenotypic values for observed production were determined for each individual using Eq. [1] and [2]. Genotypes for production potential and resistance in the offspring of selected parents were determined as the average of their parental genotypes plus a Mendelian sampling term.

The additive genetic variance explained by the QTL represents a fraction $p_m$ of the total additive genetic variance for resistance, $\sigma^2_{AR}$, under infectious circumstances. The variance of the total QTL effect in the population ($\sigma^2_{QTL}$), therefore, represents the same fraction $p_m$ of the total additive genetic variance. The QTL were assumed to have been accurately mapped, so there was no recombination between genetic marker and the QTL. The QTL effects sampled from $\sigma^2_{QTL}$ and genotypes for resistance were defined as $(1 - p_m) \times$ the QTL effect.

### *Population and Parameters*

The population consisted of 384 animals, of which 50% were female. Each generation 1 out of 16 sires were selected, as were and one out of two dams. Each sire was mated to eight dams and each dam had four offspring, two male and two female, that survived until reproduction. Selection was performed for 50 generations.

The heritability for production potential was assumed to be 0.3, with initial mean 100 and phenotypic variance of 225. The initial mean for resistance was 30, with a phenotypic variance of 36. The heritability for resistance varied: 0.1, 0.3, or 0.5. The fraction of additive genetic variance explained by the markers also varied: 10, 25, or 50%. The thresholds were three phenotypic SD for R apart and were chosen such that in the first generation approximately 17.5% of the animals had an observed production greater than zero. In the first generation, 82.5% of the population had a level of resistance below the lower threshold, so that extreme situations could be explored.

## Results

### *Comparing Selection Strategies*

Figure 1 shows population means for observed production, production potential, and resistance for 50 generations of mass selection on observed production, as presented by Van der Waaij et al. (2000). When resistance is low (in the initial generations), selection for observed production initially results in an increase in resistance, rather than in production potential. With an increasing level of resistance, selection on observed production results in an increase in both resistance and production potential. As soon as resistance has reached values above the upper threshold, selection on observed production becomes equal to selection on production potential.

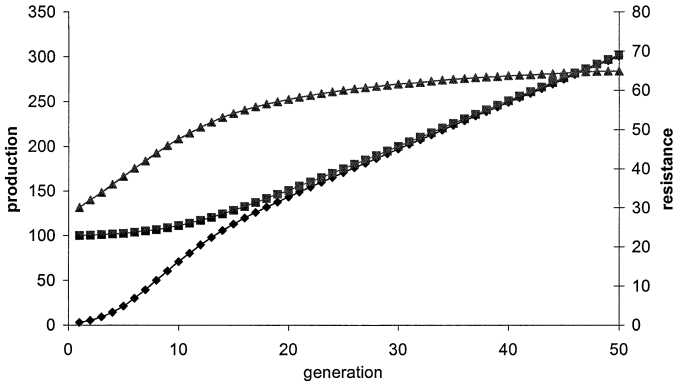


**Figure 1**. Population means for Pp (■), R (▲), and Po (◆) during 50 generations of mass selection on Po, under continuous infection pressure and for $h^2_R = 0.3$.

Figure 2 shows results for observed production (closed symbols) and resistance (open symbols) during 50 generations of selection on predicted production when the total QTL effect for resistance explained 10, 25, or 50% of the additive genetic variance. The results are expressed as deviations from results for mass selection on observed production under constant infection pressure, where the heritability for resistance was equal to 0.1 (2a), 0.3 (2b), or 0.5 (2c).

A general finding from this study is that marker-assisted selection is most successful when the heritability for the trait is low, in agreement with previous studies of marker-assisted selection (e.g., Smith and Simpson, 1986; Moreau et al., 1998). Figure 2a shows that for $h^2_R = 0.1$, when 10% of the additive genetic variance for resistance is explained by QTL, selection on predicted production results in almost the same genetic gain as mass selection. When 25 or 50% of the additive genetic variance explained by the QTL, considerably higher genetic gain for both resistance and observed production is achieved when selection is on predicted production compared to mass selection. However, Figure 2b shows that for observed production and $h^2_R = 0.3$, marker-assisted selection only remains the method of choice when 50% of the additive genetic variance is explained by the QTL.

In terms of resistance, mass selection is initially superior to selection on predicted production, for $h^2_R = 0.3$ and 0.5. When resistance approaches the upper threshold, the difference between the two selection strategies decreases again, and in the case in which 25 or 50% of the additive genetic variance is explained by the QTL, selection on predicted production becomes the method of choice. The reason for this can be found in Van der Waaij et al. (2000). Selection pressure on resistance under mass selection is ceased as soon as resistance has passed the upper threshold. The result is that animals with values for resistance just above the threshold with a high level of production will have the same chance of being selected as animals with the same production capacity but with a much higher level of resistance. Therefore, a proportion of the offspring of selected animals will have a level of resistance just below the threshold. However, during the generations in which most of the population has reached values of resistance above the upper threshold, this falling back into the less-resistant category has no influence on the genetic gain anymore (these animals will not be selected

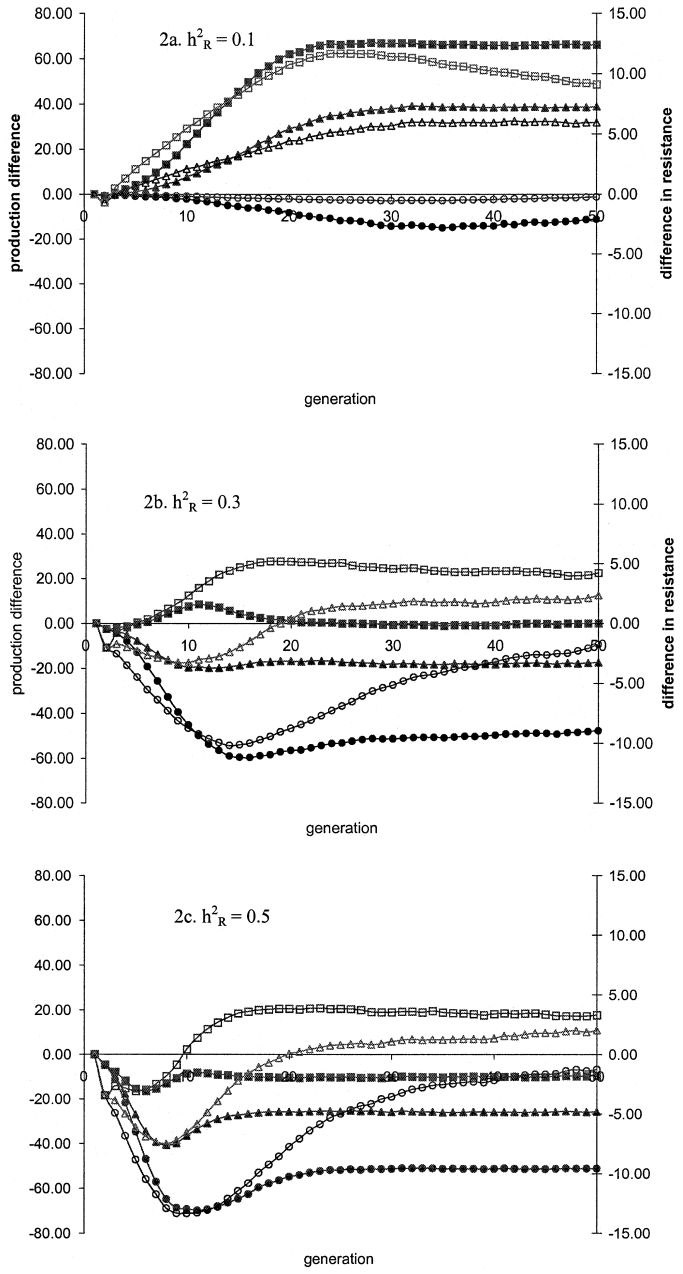


**Figure 2**. R (open symbols) and Po (closed symbols) expressing the difference between 50 generations of mass selection and selection on predicted Po in the offspring using genetic markers for resistance where 10% (●), 25% (▲), or 50% (■) of the additive genetic variance for resistance was explained by the QTL for $h^2_R = 0.1$, $h^2_R = 0.3$, or $h^2_R = 0.5$.

as parents). This situation does not occur with selection on predicted production because selection pressure on resistance remains as long as there is a possibility that a fraction of offspring will have a level of resistance below the upper threshold.

When the heritability for resistance increases further to 0.5, mass selection becomes the method of choice with regard to an increase in observed production. The initial increase in the difference in resistance between mass selection and selection on predicted production becomes more distinct and only when 50% of the genetic variance is explained by the QTL does resistance reach comparable level to the responses obtained in resistance with mass selection.

### *Intermittent Infection Pressure*

During generations without infection pressure, mass selection on observed production gives equivalent responses to mass selection for production potential. Thus, when mass selection is applied under intermittent infection pressure, selection pressure alternates between production and a combination of resistance and production, for as long as the selection candidate is not fully resistant. Selection for predicted production, however, is not affected by a change in infection pressure, provided the assumption that production level after vaccination/medication is equal to production level under uninfectious circumstances is valid. Figure 3 shows population means for resistance and observed production (as if there were infection pressure) during 50 generations of intermittent infection pressure, expressed as deviations from mass selection under constant infection pressure for $h^2_R = 0.1$, 0.3, or 0.5. Mass selection under constant infection is compared to alternated infection schemes 1-1 and 3-1 and to selection for predicted production when the QTL explained 10, 25, or 50% of the additive genetic variance.

As a result of changing selection pressure due to intermittent infection pressure, differences in gain in resistance and observed production do not follow a smooth trajectory for the intermittent infection pressure scenario when mass selection is applied, especially when the heritability for resistance is high (Figure 3). Conversely, when selection is on predicted performance, the selection pressure is not influenced by the absence of infection pressure. For all three heritabilities for resistance considered here, intermittent infection pressure always decreases the genetic gain for resistance because selection pressure is ceased during generations without infection pressure. When infection pressure is absent during half of the generations, selection on predicted production becomes the method of choice for all heritabilities for resistance considered here, when 25 or 50% of the genetic variance is explained by the QTL. In the long term, and when three generations with infection are alternated with one without infection pressure, selection on predicted production becomes the method of choice for QTL that explain 25 or 50% of the genetic variation.

The general pattern for responses in observed production in the short term is comparable to that for resistance. Important differences arise in the long term, where an increase in resistance no longer has a significant influence on observed production and mass selection, both under constant and intermittent infection pressure, becomes the method of choice. The rea-

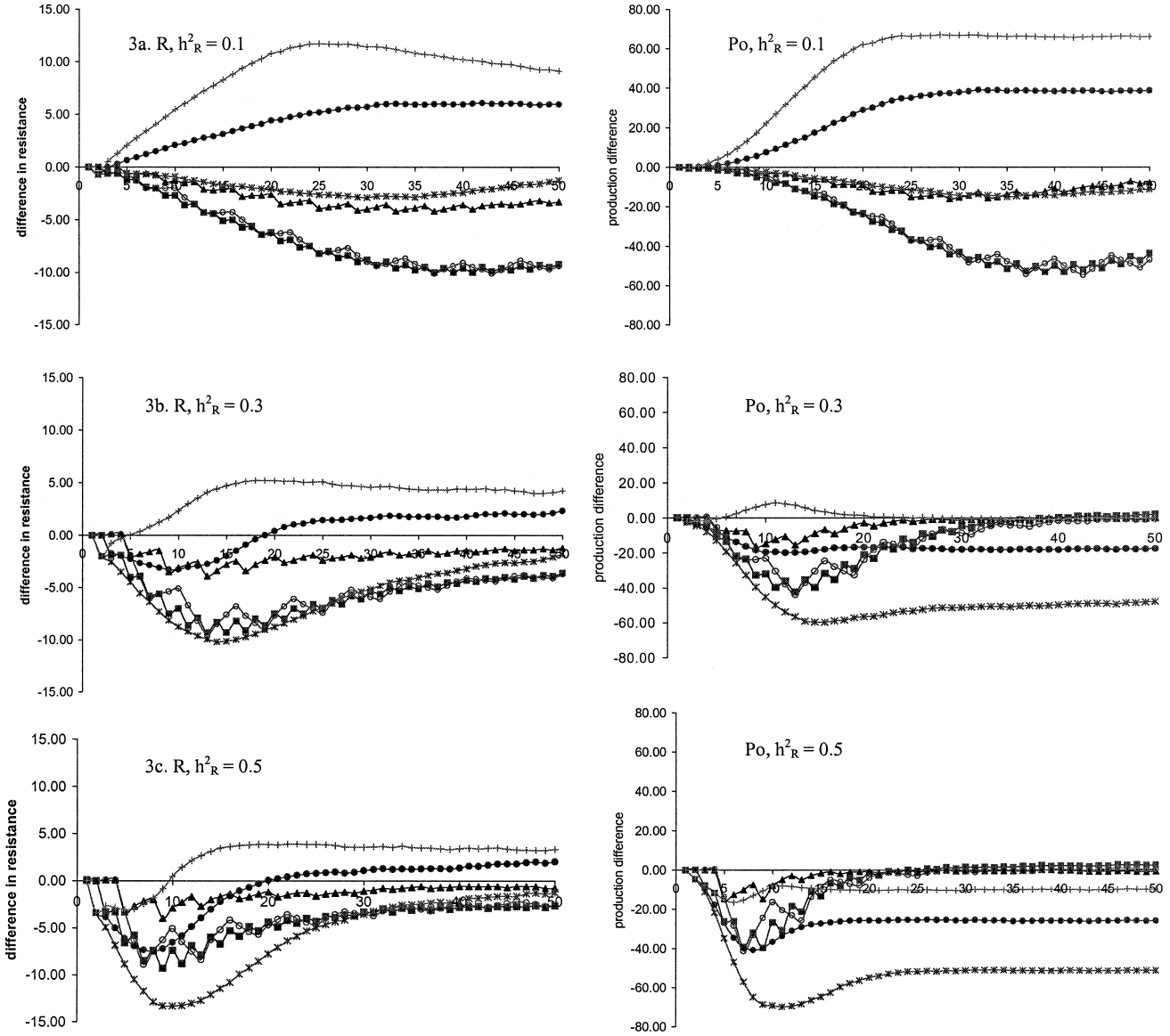


**Figure 3**. Resistance (left) and observed production (right) as deviations from mass selection on Po under continuous infection pressure for alternative intermittent schemes 1-1 (■), 3-1 (▲), or 3-3 (○), or selection on predicted production when 10% (*), 25% (●), or 50% (+) of the additive genetic variance is explained by the QTL. Results are shown for resistance heritabilities of 0.1, 0.3, or 0.5.

son for this is that in the case of mass selection all selection pressure is placed on production potential, whereas with selection for predicted production part of the selection pressure remains on resistance until all offspring have resistance above the upper threshold.

## Discussion

*General Features and Assumptions.* In the present article, the use of QTL for disease resistance in selection for increased production under infection pressure is evaluated and compared to mass selection for constant as well as intermittent infection pressure. Results show that selection on predicted production, making use of genetic markers that are linked to multiple QTL affecting resistance, can, under some circumstances, be a good alternative to mass selection for increasing production and resistance simultaneously. The advantages of marker-assisted selection are that it is no longer necessary to withhold animals from vaccination or treatment with medication after infection until measurements are taken for observed production, or even to keep them in an infected environment. We have demonstrated that, in general, the level of resistance is increased more by using QTL for resistance than it is under mass selection on performance. However, under the assumptions made in the model, genetic gains in observed production are only comparable, or superior to, mass selection when the heritability for resistance

is low. If the selection pressure is intermittent, then mass selection to improve production under constant infection pressure becomes less efficient.

When comparing mass selection on observed production to index selection on the predicted production, it was assumed that treatment with medication would increase observed production to production potential in cases in which the animal was not fully resistant. In reality, in most situations this assumption is too optimistic and the infection, for example a trypanosomosis infection, may still result in an increased requirement of energy and a decreased feed intake (Van Dam, 1996), at the expense of production. Also, energy may be required to repair the damage done during periods when the animals were infected. Medication will restore production loss to some extent, but the resulting production level may still be lower than production potential. The consequence of the fact that the actual production level may be lower than production potential is that, depending on the population level of resistance, indirectly more selection pressure will be put on resistance (part of the production is still influenced by lack of resistance, i.e., observed production is still not equivalent to production potential).

When the animals are kept in an uninfected environment, the model may be a closer approximation to reality. However, it should be realized that the model not only describes the effect of resistance to the infection under consideration, but actually a combination of effects of all environmental influences that are continuously present, including other infections, husbandry system, climatic aspects, and nutritional state. Therefore, depending on the recording of the phenotype, QTL for resistance may not only influence disease resistance, but also the adaptability of the animal to the environment the QTL are mapped in. An environment in which the infection under consideration is absent may also differ in some other constant environmental factors compared to the infected environment. Therefore, it is important that the QTL for resistance be mapped in the environment for which the animals are selected.

Unlike with mass selection, with selection on predicted production it is necessary to know which values of resistance coincide with the lower and with the upper thresholds. This information is needed to determine the correct predicted fractions of offspring in each of the three regions divided by the thresholds. The distance between thresholds is, among other factors, determined by the infection pressure. Intermittent selection pressure may be thought of as representing a situation in which threshold values are occasionally assigned wrongly (in the absence of infection pressure $f(R) = 1$). Results in this article show that the model is reasonably robust to incorrect threshold values; the results between constant and intermittent selection pressure only differ slightly.

*QTL Information.* In order to successfully select on predicted production, multiple QTL are required. The accuracy will decrease with increasing distance between QTL and genetic markers (increasing occurrence of recombination events) and with decreasing frequency of the QTL in the population. It was assumed that fixation and detection of QTL balance each other out so that sufficient QTL remain available to give an approximately normal distribution. In published literature, essentially two types of assumptions can be found with regard to number of QTL under selection. Some assume there are only a limited number of QTL available and after those are fixed there will be no new ones detected (e.g., Dekkers and van Arendonk, 1998). Others (e.g., Meuwissen and Goddard, 1996) assume that new QTL will be detected continually. This reasoning is based on the fact that in populations that have been under strong selection for many generations, QTL for production traits are still being detected (e.g., a QTL for milk yield in dairy cattle [Coppieters et al., 1998]). One important reason to adhere to either of the previous theories, apart from mutation rate of the QTL (Falconer, 1989), is the presence or absence of interaction between QTL. The QTL detection studies carried out so far assumed that the effect of each QTL stands alone (is additive and sometimes dominant), and possible epistatic effects with other QTL are ignored (e.g., Coppieters et al., 1998). The result of this assumption is that marker-assisted selection is assumed to lead to fixation of the QTL, and thus to a serious decrease in variance explained by the QTL. However, when assuming a very simple interaction between two QTL, as suggested by Nijhout and Paulsen (1997), a small change in genetic background (e.g., by fixation of QTL through selection) may have a large effect on the expression of (new) QTL. They showed that not only is it likely that new QTL will be detected on a regular basis (with a limitation on the number of genes involved in the trait expression, of course), but also that it is important to continue QTL detection because new QTL occur due to changes in expression during the selection process.

Whichever theory is correct, in the present study QTL that are detected first are most influential in the selection process, because selection pressure on the QTL effect (resistance) decreases with increasing level of resistance. When resistance is approaching the upper threshold, an increase in resistance is of less importance. This effect is strengthened by the fact that it is likely that the QTL with a large effect will be detected first. Only a few QTL are expected to have large effects, with many having small effects (Bost et al., 1999). Thus, the QTL with smaller effects that will be detected later will have a smaller influence not only because of their smaller size, but also due to the fact that population level of resistance is already at such a level that more emphasis is put on production. Therefore, if a change in variance due to fixation of a QTL with a large effect may occur, it is likely to be of less influence when the threshold model is applied than when a linear model is used.

The size of the total QTL effects considered in this study was varied from 10 to 50% of the additive genetic

variance, a wide range of effects. Phenotypic values for resistance as defined in this study often cannot be measured accurately, but results for several indicator traits describing resistance have been reported. Dumas et al. (2000) reported an effect explaining 46% of the phenotypic variance for stress response in rats. Stear et al. (1996) found that allelic variation at the MHC-DRB1 locus accounted for 33% of the additive genetic variance for fecal egg count in sheep. Zhang et al. (1998) found several QTL for somatic cell count in dairy cows, the largest explaining more than 27% of the additive genetic variance. The sum of QTL effects they detected for somatic cell count explained approximately 50% of the additive genetic variance, although they indicated that their estimates might be overestimated. Thus, our assumed QTL effects are within the range of values reported in the literature.

*Concluding Remarks.* This article has presented methodologies for using disease resistance QTL, under certain assumptions with regard to infection pressure. It is important to realize that although such QTL are often important and beneficial, there are also circumstances in which their use cannot be justified either in terms of potential genetic progress or cost-effectiveness.

As described by Van der Waaij et al. (2000), this model and general methodology has applications that are wider than disease resistance per se. Other important applications include environmental or metabolic stresses. A further application of this model may be to the challenge faced by pig and chicken breeding companies that select animals under high health status conditions for production in more challenging commercial environments.

## Implications

Simultaneous genetic gain is considered for both production and resistance to a disease characterized by constant infection pressure, where genetic markers (i.e., QTL) for resistance aid the selection of animals with enhanced resistance. Selection responses are quantified by stochastic simulation. The model assumes some simplifications compared to reality. Results suggest that only when the heritability for resistance is low does selection on predicted production using resistance QTL result in greater gain for resistance and observed production than mass selection on observed production under constant infection. Intermittent infection pressure reduces the effectiveness of mass selection, increasing the relative value of QTL for resistance. Selection on predicted production requires the availability of multiple, accurately mapped QTL, which should soon be technically possible. Mapping QTL requires phenotypic observations, so (some) animals will need to be infected to map resistance QTL.

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