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Statistical models for genotype by environment data: from conventional ANOVA models to eco-physiological QTL models

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Abstract. To study the performance of genotypes under different growing conditions, plant breeders evaluate their germplasm in multi-environment trials. These trials produce genotype × environment data. We present statistical models for the analysis of such data that differ in the extent to which additional genetic, physiological, and environmental information is incorporated into the model formulation. The simplest model in our exposition is the additive 2-way analysis of variance model, without genotype × environment interaction, and with parameters whose interpretation depends strongly on the set of included genotypes and environments. The most complicated model is a synthesis of a multiple quantitative trait locus (QTL) model and an eco-physiological model to describe a collection of genotypic response curves. Between those extremes, we discuss linear-bilinear models, whose parameters can only indirectly be related to genetic and physiological information, and factorial regression models that allow direct incorporation of explicit genetic, physiological, and environmental covariables on the levels of the genotypic and environmental factors. Factorial regression models are also very suitable for the modelling of QTL main effects and QTL × environment interaction. Our conclusion is that statistical and physiological models can be fruitfully combined for the study of genotype × environment interaction.

Additional keywords: AMMI-model, crop growth model, factorial regression, genotype by environment interaction, multi-environment trial, QTL by environment interaction.

Introduction

A major objective in many advanced plant breeding programs is to assess the suitability of individual crop genotypes for agricultural purposes across a range of agro-ecological conditions. To this purpose, breeders perform so-called multi-environment trials. In a multi-environment trial, a set of genotypes is evaluated across several environments that hopefully represent the environmental range across which the genotypes should partially (specific adaptation) or wholly (wide adaptation) perform well. The performance of genotypes in multi-environment trials is analysed by statistical models developed to describe and interpret genotype × environment data. The statistical analysis should provide estimates for parameters that indicate both how well genotypes perform on average across the environmental range and how well they perform in specific environmental conditions. Traditionally, the statistical parameters used by breeders to characterise genotypic responses across environments were largely devoid of physiological meaning. More recently, it has become popular to use statistical models whose parameters relate better to physiological knowledge and that permit varying degrees of integration between statistical and physiological approaches to description and prediction of genotypic responses across environments. In the context of plant breeding, a landmark publication strongly advocating the integration of statistical and physiological approaches is the book by Cooper and Hammer (1996).

This paper discusses various classes of statistical models for the analysis of genotype × environment data. All the models can be interpreted in terms of response functions for individual genotypes to environmental variables. The differences between the models reside in the amount of genetic and physiological characterisation of the genotypes, the amount of physical and meteorological characterisation of the environments, and the complexity of the response curves. We intend to show that statistical and physiological models for the description of genotype × environment data can be reconciled and combined in a fruitful way.

The additive model in quantitative genetics and plant breeding

Within plant breeding, a tradition exists to describe phenotypic responses across environments in terms of

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statistical parameters that have well-defined statistical properties, but that are hard to interpret in physiological terms. The dominant quantitative genetic paradigm in plant breeding dictates models for phenotypic expression to consist of sums of terms that are indexed by genotypes, environments, or combinations of both. The simplest model for the description of phenotypic responses across environments, the additive model, contains only single indexed terms. For the expected phenotypic response for genotype i ($i = 1, \ldots, I$) in environment j ($j = 1, \ldots, J$), μ_{ij}, we write:

$$\mu_{ij} = \mu + G_i + E_j \qquad (1)$$

where μ is the general mean, G_i is the genotypic main effect expressed as a deviation from the general mean, and E_j is the environmental main effect, again expressed as a deviation from the mean.

Although the statistical description of the additive model suggests some complexity, the above model merely states that we might try to describe the phenotypic responses for a set of genotypes as a set of parallel straight lines, where the differences between the responses are given by the differences between the genotypic main effects. To illustrate this, we consider the increase in the mean response for a genotype i, when going from environment j to j*, where we assume that j* represents the better environment ($E_{j^*} > E_j$) : $\mu_{ij^*} - \mu_{ij} = E_{j^*} - E_j$. It is obvious that all genotypes will show the same increase in phenotypic response when going from the inferior environment j to the superior environment j*. When the environmental main effect is interpreted as an indicator of environmental quality, we might say that all genotypes exhibit the same sensitivity to the environment. To emphasise the parallel response character of the additive model, we can write $\mu_{ij} = G_i' + \beta_i' E_j$, where $G_i' = \mu + G_i$, the predicted mean performance for genotype i across environments, and the slope β_i' is equal to 1 for all genotypes.

The most curious property of the additive model is that its parameters suggest a reference to genotypic and environmental entities outside the model, i.e. there appear to be things or processes that might be called genetic (genotypic) in nature as well as environmental. However, the genotypes in the additive model are nothing more than the levels of a nominal variable, where the idea is that the major differences between the levels of that factor reside ultimately in differences in DNA composition. In the additive model, the environment is a collection of discrete sets of conditions under which the plants pertaining to particular genotypes have been grown. The parameters G_i and E_j are estimated by averaging over phenotypic observations, and at no point in this process does something evidently genetic or environmental enter the calculations. For balanced data (e.g. all genotype × environment combinations were observed equally often, without missing values), the estimate for the main effect of genotype i follows from the average across environments of the phenotypic observations indexed by i. Likewise, the estimate for the main effect of environment j follows from the average across genotypes of observations indexed by j. Thus, genotypic main effects depend on the collection of environments that were included in the experiments, and environmental main effects depend on the genotypes that were included. Suppose we evaluate yield for a set of genotypes that consists of 2 subsets: one subset of genotypes that are tolerant to a major stress factor and another subset of genotypes that are susceptible to the same stress factor. Genotypic main effects in the tolerant and susceptible subset will, other things being equal, be of similar magnitude as long as the particular environmental stress factor does not occur in the sample of environments included in the trials. In contrast, when in at least some of the environments the pertinent stress factor does occur, the susceptible genotypes will rank lower than the tolerant ones.

An equivalent argument can be constructed for the environments. Environments may differ in nutrient and water availability, but without genotypic variation in sensitivity to the quality of the environment, the better environments will not be recognisable for their higher yield, i.e. higher environmental main effects. Therefore, strictly speaking, neither the genotypic main effects nor the environmental main effects represent entities that exist outside of the collection of genotypes and environments that were included in the trials and the model for which they have been estimated. The main purpose of the additive model is to interpret phenotypic differences in terms of differences between the levels of the genotypic factor on the one hand and between levels of the environmental factor on the other hand for the included sets of genotypes and environments. Of course, the genotypes and environments in the trials may be chosen to be representative of some population of interest. For the environments, we then speak of the target population of environments (Comstock 1977; Chapman *et al*. 2000*a*, 2000*b*, 2000*c*). For the latter case, the environmental main effects are often assumed to follow a normal distribution. Whatever the statistical details, it may be clear that it will be difficult to encounter in an individual plant the physiological counterpart of its genotypic main effect.

Models for interaction using phenotypic characterisations of the environment

The additive model is an elementary model that is more important as a didactical tool to introduce statistical models for genotype × environment data than as a serious description of such data. The additive model provides a null model against which to test models that are more complicated with terms for genotype × environment interaction. Genotype × environment interaction occurs whenever genotypes react differently to environmental changes. So, whenever the difference in phenotypic performance between two environments j and j* varies between 2 genotypes i and i*, i.e. $\mu_{ij^*} - \mu_{ij} \neq \mu_{i^*j^*} - \mu_{i^*j}$, the additive model will be inadequate and a more elaborate

model should be formulated. Traditionally, the additive model is extended to a full interaction model with double indexed genotype × environment terms for each combination of genotype and environment:

$$\mu_{ij} = \mu + G_i + E_j + (GE)_{ij} \quad (2)$$

In the full interaction model there are as many independent parameters as genotype × environment combinations and, from the point of view of parsimony, little has been accomplished by fitting this model to the data. Predictions of phenotypic responses for environments that were not in the set of trial environments are impossible, as there will be no estimates for the particular $(GE)_{ij}$ terms. Compare this with the situations for which the additive model provides a good fit. In those cases, rough predictions are possible as long as the quality of the new environment can be ranked as being in between 2 environments that were part of the multi-environment trial.

An alternative, more attractive extension of the additive model, which, like the additive model, describes phenotypic responses as straight lines, but allows for differential environmental sensitivity between genotypes, is the regression on the mean model, popularised by Finlay and Wilkinson (1963). The philosophy behind this model is that in the absence of explicit physical or meteorological characterisations of an environment, a good approximation to the general biological quality of the environment is given by the average phenotypic performance across the genotypes. The phenotypic responses of individual genotypes are then regressed on the average performance, and the genotype × environment interaction (GEI) expresses itself by differences in the slopes between the genotypes.

An elaborate way to write the regression on the mean model, that shows the relation with the full interaction analysis of variance model, is:

$$\mu_{ij} = \mu + G_i + E_j + \beta_i E_j \quad (3)$$

The GEI is modelled as differential genotypic sensitivity, represented by the parameters β_i, to the environmental characterisation E_j, with the average sensitivity being zero. A reformulation of the model makes evident the non-parallel straight lines nature of the regression on the mean model $\mu_{ij} = \mu + G_i + E_j + \beta_i E_j = (\mu + G_i) + (1 + \beta_i)E_j = G_i' + \beta_i' E_j$, where the average sensitivity now will be unity; $\overline{\beta_i'} = 1$. When all β_i are zero, or all β_i' are 1, the regression on the mean model reduces to the additive model. Alternatively, the regression on the mean model will be equivalent to the full interaction model when $(GE)_{ij} = \beta_i E_j$ for all genotype × environment combinations.

The estimate for the sensitivity, or responsiveness, to the environment of individual genotypes depends on the average potential of the genotypes to change in relation to the environmental conditions. Therefore, the interpretation of the magnitudes of individual genotypic sensitivities should take into account the composition of the genotype and environment sets included in the multi-environment trial. For example, one susceptible genotype in a collection of otherwise tolerant genotypes evaluated under environmental conditions that include at least one instance of the pertinent stress will have a far higher estimated environmental sensitivity than the same susceptible genotype evaluated within a predominantly susceptible set of genotypes. Table 1 shows an example of this principle for 2 fictitious data sets.

Table 1. Illustration of how genotypic sensitivity depends on composition of genotype set

Set 1 contains predominantly genotypes tolerant to stress and set 2 predominantly susceptible genotypes. Sensitivities can be calculated by dividing the difference in individual performance between non-stress and stress by the average difference for the corresponding set of genotypes

Genotype	Characterisation	Performance in non-stress environment	Performance under stress	Sensitivity
Set 1				
A	Tolerant	7	6	0.5
B	Tolerant	7	6	0.5
C	Tolerant	7	6	0.5
D	Susceptible	8	3	2.5
Average Set 1	Mainly tolerant	7.25	5.25	1.0
Set 2				
A	Tolerant	7	6	0.25
D	Susceptible	8	3	1.25
E	Susceptible	8	3	1.25
F	Susceptible	8	3	1.25
Average Set 2	Mainly susceptible	7.75	3.75	1.0

Like the additive model, the regression on the mean model can be used for prediction to the extent that new environments can be ranked with respect to the environments included in the trial set.

The regression on the mean model partitions the genotype × environment interaction term, $(GE)_{ij}$, in the full interaction model into a part due to regression on the environmental main effect (environmental index), $\beta_i E_j$, and a residual $(GE)^*_{ij}$. This residual is usually interpreted as a random variable with zero mean, leading to the absence of this term in the expectation, μ_{ij}. The statistical success of the regression on the mean model depends on the proportion of genotype × environment interaction that is described by the differential environmental sensitivity of the genotypes, or, equivalently, by the quality of the environmental effect as a reflection of the environmental forces that cause phenotypic differences between genotypes. The regression on the mean model provides only limited flexibility for describing GEI, because of its rather specific, 1-dimensional incorporation of the environmental factors affecting the phenotypic responses. However, other models from the model class of which the regression on the mean model is a member, the class of linear-bilinear models (Gabriel 1978, 1998; van Eeuwijk 1995*a*; Denis and Gower 1996; Crossa and Cornelius 2002), allow considerably more flexible characterisations of the environment. All these models describe GEI by differential genotypic sensitivities to environmental characterisations that are derived from the phenotypic data themselves.

Linear-bilinear models consist of sums of single indexed additive and multiplicative terms. In the regression on the mean model, using the regression formulation, $G_i' + \beta_i' E_j$, the linear part of the model is given by G_i', whereas the bilinear part is equal to $\beta_i' E_j$. The term $\beta_i' E_j$ contains genotypic and environmental parameters that need to be estimated simultaneously. The name bilinear models stems from the observation that these models become standard linear models in the genotypic parameters upon fixation of the environmental parameters and vice versa. This property also forms the basis of a general estimating procedure for the parameters (Gabriel and Zamir 1979; van Eeuwijk 1995*b*; Gabriel 1998).

In comparison with the regression on the mean model, more flexible linear-bilinear models for the modelling of GEI can be constructed by the inclusion of additional bilinear terms. A popular example of a linear-bilinear model with a varying number of bilinear terms for the description of GEI is the additive main effects and multiplicative interaction effects model, best known under its acronym AMMI (Gollob 1968; Mandel 1969; Gabriel 1978; Gauch 1988). The model can be formulated as:

$$\mu_{ij} = \mu + G_i + E_j + \sum_{k=1}^{K} a_{ki} b_{kj} \qquad (4)$$

where a_{ki} and b_{kj} are genotypic and environmental parameters (scores) for the bilinear term k, and where K indicates the number of multiplicative terms necessary for an adequate description of the genotype × environment interaction. Following the same logic as for the regression on the mean model, the genotypic scores, a_{ki}, can be interpreted as sensitivities or responsiveness, and the environmental scores, b_{kj}, are environmental characterisations. The environmental scores for the first bilinear term represent the best environmental characterisation possible for the description of the genotype × environment interaction in terms of differences in genotypic sensitivity. The second bilinear term represents the second best environmental characterisation, etc. The environmental characterisations in bilinear terms are acquired by minimisation of a least-squares criterion, and may not always have an immediate physiological interpretation. Still, regressing the environmental scores on explicit environmental measurements usually allows the genotype × environment interaction to be related to physiological processes (Vargas *et al*. 1999).

Models for interaction using explicit environmental characterisations

Bilinear models for interaction are very useful for a first round of exploratory analyses in which differences between genotypes are modelled by sensitivities to hypothetical environmental characterisations that describe a maximum amount of the genotype × environment interaction. Whether the results of analyses by bilinear models contain any physiological interest depends on the relation that the environmental main effects and scores bear to a description of the environment in terms of external, physical, and meteorological variables. For example, suppose that it is concluded from the analysis of a particular data set that the regression on the mean model gives an adequate description of the genotype × environment interaction and that the environmental main effect is primarily driven by average daily temperature, T_j. We then think of E_j in the regression on the mean model as a function of T_j, $E_j = f(T_j)$, and write: $\mu_{ij} = G_i' + \beta_i' E_j = G_i' + \beta_i' f(T_j)$. The latter model would definitely be a lot closer to the kind of models that physiologists are used to working with than the purely phenotypic regression on the mean model. In addition, the latter kind of model would allow the phenotypic responses to be non-linear, i.e. to become response curves as exponential, logistic, Gompertz, Gaussian, or some other suitable response curve, as long as the curve parameters are genotype-independent.

The simplest way of replacing the environmental effect by a function of an explicit environmental variable, is by using the identity function for f(.). For example, describing the interaction as driven by temperature would lead us to $\mu_{ij} = G_i' + \beta_i' z_j$, where z_j is the temperature in environment

j. The extension to more than one environmental variable is straightforward. Suppose that the genotype × environment interaction is driven by both the average temperature, z_{1j}, and the amount of rainfall, z_{2j}, then the following model might be appropriate: $\mu_{ij} = G_i' + \beta_{1i}' z_{1j} + \beta_{2i}' z_{2j}$, where β_{1i}' and β_{2i}' are the sensitivities to temperature and rainfall, respectively.

Contrary to what physiologists would do, plant breeders customarily want to correct the phenotypic data for the environmental main effect, and thereby concentrate on that part of the phenotypic differences that is caused by genotype-related sources of variation (G_i and $(GE)_{ij}$). Plant breeders are not particularly interested in a (physiological) model for the trial mean; they especially want to understand the differences between genotypes. When we follow that convention and include the environmental main effect, the above model becomes:

$$\mu_{ij} = \mu + G_i + E_j + \beta_{1i} z_{1j} + \beta_{2i} z_{2j} \quad (5)$$

The resemblance of the latter regression-like model with a linear-bilinear model with two bilinear terms for the interaction, $\mu_{ij} = \mu + G_i + E_j + a_{1i} b_{1j} + a_{2i} b_{2j}$, is evident. The environmental scores b_{1j} and b_{2j} are, theoretically, the best environmental covariables for explaining GEI, but for a physiological understanding of the GEI, these scores should be interpreted in terms of measured or simulated environmental characterisations. One way to do so would be by regressing the environmental scores on a set of environmental covariables. In exceptional cases, the environmental scores of the linear-bilinear model can be replaced by environmental covariables without loss of descriptive adequacy for the GEI. In such cases, a physiology-inspired description of the GEI will coincide with the best statistical description for the particular data.

Statistical models for phenotypic responses across environments that describe genotype × environment interaction by differential sensitivity to explicit environmental variables belong to the class of factorial regression models (Denis 1988; van Eeuwijk *et al*. 1996). The name is derived from the inclusion of covariables on the levels of the classifying factors in analysis of variance models. The critical issue for factorial regression models is the choice of covariables. In former days, in the absence of explicit information about the environment, the regression on the mean model, or another linear-bilinear model, was an obligatory choice. As a continuous registration of the environment has come within reach of many plant breeding trials, the question nowadays has become how to summarise the most relevant features of the environment from the point of view of genotype × environment interaction (Cooper and Hammer 1996). Exclusively statistical approaches as variable subset-selection procedures are not very satisfactory, because they result mostly in physiologically difficult-to-interpret models. The most promising way forwards seems to be the use of physiological knowledge to delimit the vast amount of potentially useful sets of environmental covariables. Examples of the use of factorial regression guided by physiological knowledge to analyse adaptation and genotype × environment interaction in barley can be found in Voltas *et al*. (1999*a*, 1999*b*).

Instead of physical measurements of the environment, one could also use simulated characterisations of the environments in a multi-environment trial. Crop growth models can be used to integrate environmental information over the growing season, which may result in a characterisation of the environments in terms of different stress classes (Chapman *et al*. 2000*b*). This type of environmental characterisation can then be introduced as a categorical variable in a factorial regression model. Of course, when a crop growth model produces a quantitative stress index, this index could also be included in a factorial regression to model GEI. Note that although environmental covariables enter the factorial regression models linearly, there is no restriction on the phenotypic responses of having to be linear as well, as also quadratic and higher order terms can be included into the model. Furthermore, response surfaces based on multiple environmental covariables are equally feasible, provided the data contain enough information for the estimation of all the parameters.

Models for interaction using explicit genotypic and environmental characterisations

The inclusion of covariables on factor levels in analysis of variance models for the description of GEI is not only useful for the environmental factor(s), but is equally recommendable for the genotypic factor(s). For example, a laboratory test may have been developed to assess the tolerance of a set of genotypes against a particular stress factor and one wants to include the results of such a test in an analysis of variance model for a multi-environment trial on yield to describe genotypic differences dependent on the environment. Assume the values of the laboratory tests are expressed by the genotypic covariable x, with values x_i, then we can incorporate this covariable in the 2-way analysis of variance model as follows:

$$\mu_{ij} = \mu + G_i + E_j + x_i \rho_j \quad (6)$$

The parameters ρ_j then relate to the severity of the particular stress in environment *j*.

Genotypic covariables can also be used for the description of differences in genotypic means across environments:

$$\mu_{ij} = \mu + x_i \rho + G_i^* + E_j \quad (7)$$

where G_i^* is a residual genotypic main effect that should be smaller when the description by x_i is more successful. An interesting application of this type of factorial regression model is in the detection and localisation of quantitative trait loci (QTLs). The regression-based approaches to QTL

mapping, as initiated by Haley and Knott (1992), can be seen as a form of factorial regression with genotypic covariables that are functions of marker genotypes and the type of QTL effect (additive, dominance, epistasis). Consider a co-dominant marker that can assume the genotypes MM, Mm, and mm. A genetic covariable, or genetic predictor, for estimating the additive genetic effects of a putative QTL at the position of this marker can be constructed by giving the predictor, x, individual values, x_i, that correspond to the number of M alleles in the specific plants: $x_i = 2$ for genotypes of the MM type, $x_i = 1$ for Mm, and $x_i = 0$ for mm. For statistical reasons, it is often preferable to work with the equivalent set of values of 1 for MM, 0 for Mm, and -1 for mm when estimating the additive genetic effects of a QTL, especially when one also wants to include a genetic predictor for dominance effects, where the latter has typically the value 1 for Mm genotypes, and 0 for MM and mm genotypes. By constructing genetic predictors at all marker positions, a genome scan for QTLs by marker regression can be performed. Effectively, the genome scan consists of the fitting of model (7), with x_i derived from local marker genotype information, while testing for the QTL effect, ρ. Genetic predictors in between marker positions, necessary for simple interval mapping, can be constructed as functions of the probabilities of QTL genotypes given flanking markers. Lynch and Walsh (1998) provide an introduction to procedures for constructing genetic predictors, and Jiang and Zeng (1997) present a very general algorithm for all kinds of biparental segregating populations. Composite interval mapping requires the inclusion of so-called co-factors, markers that correct for QTLs elsewhere on the genome. These co-factors can be chosen to be the genetic predictors corresponding to the QTLs identified during a genome scan by marker regression or simple interval mapping. In model form we write $\mu_{ij} = \mu + \sum_{c \in C} x_c \rho_c + x_i \rho + G_i^* + E_j$, where the terms $x_c \rho_c$ correct for putative QTLs elsewhere on the genome, C is the full set of such putative QTLs, and $x_i \rho$ is the QTL under test.

In the framework of factorial regression, modelling of QTL × environment interaction is a natural extension of modelling main effect QTLs, i.e. QTLs that are supposed to have constant expression across environments. A model with a QTL main effect and QTL × environment interaction at the same location in the genome can be written as:

$$\mu_{ij} = \mu + x_i \rho + G_i^* + E_j + x_i \rho_j + (GE)_{ij}^* \qquad (8)$$

The $(GE)_{ij}$ from the analysis of variance model is partitioned in a part due to differential QTL expression, $x_i \rho_j$, and a residual, $(GE)_{ij}^*$, that is usually taken as random and for that reason then disappears from the expression for the expectation. In the light of QTL × environment interaction, the parameter ρ_j adjusts the average QTL expression across environments, ρ, to a more appropriate level for the individual environment j. The QTL × environment interaction parameters, ρ_j, can themselves be regressed on an environmental covariable, z, in an attempt to link differential QTL expression directly to key environmental factors. The QTL × environment interaction term $x_i \rho_j$ is replaced by a regression term $x_i(\lambda z_j)$ and a residual term $x_i \rho_j^*$:

$$\mu_{ij} = \mu + x_i \rho + G_i^* + E_j + x_i(\lambda z_j) + x_i \rho_j^* + (GE)_{ij}^* \qquad (9)$$

The residual term $x_i \rho_j^*$ will disappear from the expectation when ρ_j^* is assumed to be random. The parameter λ is a proportionality constant that determines the extent to which a unit change in the environmental covariable, z, influences the effect of a QTL allele substitution.

From a breeding and physiological point of view, the above model is an interesting option, because it allows the prediction of differential genotypic responses to environmental changes from marker information characterising the genotypes and environmental covariables characterising the environment. van Eeuwijk *et al*. (2001*b*, 2002) give an example of differential QTL expression in relation to the minimum temperature during flowering for yield in maize data from the CIMMYT program on drought stress. Malosetti *et al*. (2004) analysed yield data from the North American Barley Genome Project with added environmental information. QTL × environment interaction at chromosome 2H was found to depend on the temperature range during heading (Fig. 1). A QTL allele substitution increased/decreased yield with 0.112 ton/ha for every degree Celsius that the temperature range increased.

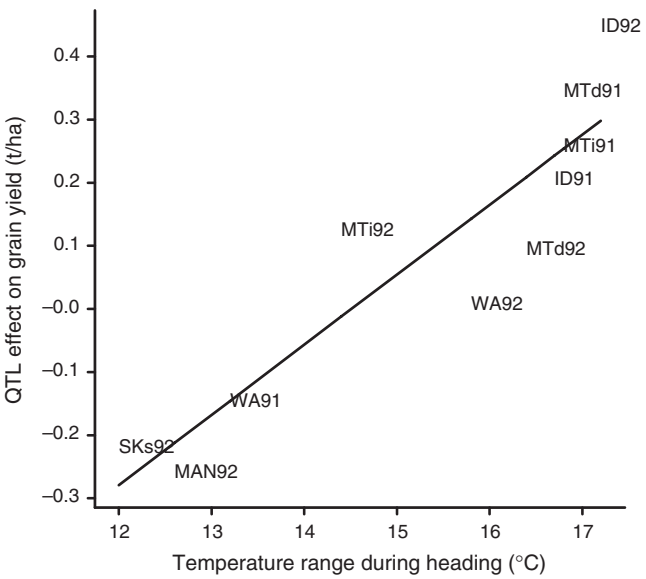

Fig. 1. Regression of QTL × environment interaction effects for grain yield in barley on the environmental covariable, temperature range during heading (chromosome 2H). Yield data stem from 10 environments included in the North American Barley Genome Project. For those environments, additional environmental information was collected.

Models for GEI based on QTLs whose expression is a function of environmental covariables may help to solve the recurrent discussion on the extent to which input parameters for crop growth models should be 'genetic'. The point of discussion is the idea that input parameters that exhibit GEI are not 'genetic', or not 'genetic' enough, to guarantee the successful application of crop growth models. However, as far as this dispute relates to predictability of physiological parameters and yield from genetic and environmental information, there should not be any problem with GEI in input parameters, as long as the GEI follows from differential QTL expression conditional on environmental covariables. In the latter case, the GEI can be described by the product of genetic predictor and environmental covariable, $x_i \lambda z_j$, and requires only an estimate of the unproblematic proportionality constant λ.

Models for response curves

A drawback of the QTL models described in the previous paragraph may be that they are linear in the parameters, whereas most physiological and developmental processes behave essentially in a non-linear manner in relation to the environment. Although polynomial expansions can provide good approximations to those non-linear functions, an intrinsically non-linear approach will usually be preferable. Wu *et al*. (2002) formulated a 2-step approach that acknowledges the non-linearity of response curves for physiological traits, but they still use linear QTL models for the parameters of those curves. Firstly, they fit non-linear functions to growth data for each of the genotypes separately and then analyse the estimated parameter vectors jointly in a multivariate composite interval mapping procedure. A fully non-linear approach to physiological response curves is presented by Ma *et al*. (2002). Their methodology is based on mixture models and an EM algorithm for estimation. The paper contains an example for logistic growth curves in poplar. The authors claim that their intrinsically non-linear approach to the unravelling of the genetic basis of growth curves has higher power than alternative approaches. In M. Malosetti and F. A. van Eeuwijk's unpublished work, the philosophy proclaimed by Ma *et al*. (2002) has been translated into the slightly less demanding non-linear mixed model framework. The process of senescence in potato was modelled by a logistic curve for individual diploid potato genotypes stemming from a biparental cross. The model for the expectation of the state of senescence for genotype i at time point j was $\mu_{ij} = A + \frac{C}{1+e^{-b_i(z_j - m_i)}}$, where z_j is the time from planting to observation. The lower asymptote, A, and the difference between lower and upper asymptote, C, were the same for all genotypes, and the location of the inflection point, m_i (i.e. the time at which the process of senescence reaches the point half-way between the upper and lower asymptote), and the slope parameter at this point, b_i (i.e. the maximum rate of senescence), were genotype specific. The values for slope and inflection points were modelled on genetic predictors inside the non-linear mixed model, i.e. different QTL alleles had different average slopes and inflection points, and the genotype-specific deviations from those averages were given a bivariate normal distribution. Various QTLs were detected for both slopes and inflection points. As the QTLs for slopes and inflection points were largely uncorrelated, rate and timing of the senescence process seemed amenable to independent genetic improvement. Figure 2 shows the allelic effects of a QTL with an effect principally on the location of the inflection point and another QTL affecting mainly the slope of the senescence curve.

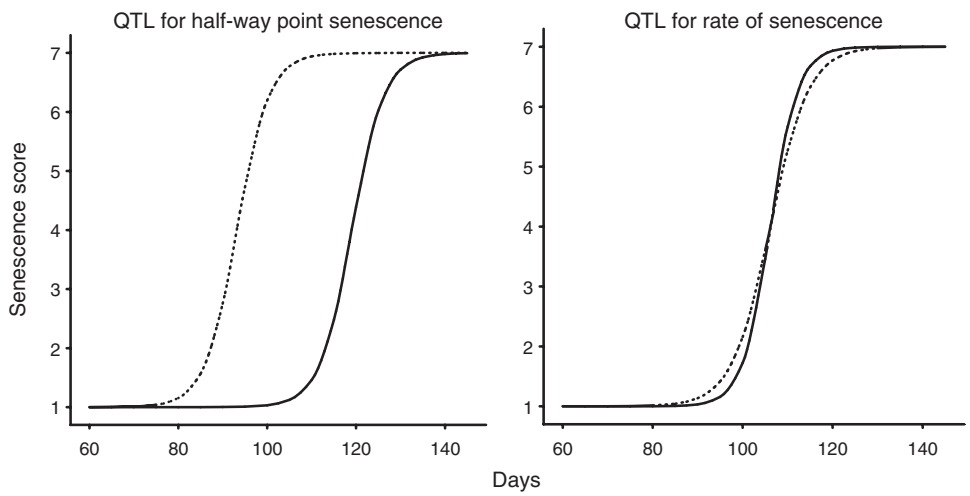

Fig. 2. Demonstration of QTL allele effects working principally on location (left) and slope (right) of senescence curves in potato. Solid curves represent QTL genotype as occurring in one parent, and dotted curves represent the other parent.

The non-linear QTL models of Ma *et al*. (2002) and M. Malosetti and F. A. van Eeuwijk (unpublished data) provide powerful methods for eco-physiologically inspired genetic models for differential phenotypic expression in relation to environmental variables and (developmental) time. However, it cannot be denied that these models require a considerable amount of statistical skill for successful application. Therefore, it is reassuring that the simpler 2-step approach that first estimates the parameters in non-linear response curves for individual genotypes by standard non-linear regression methodology and next searches for the genetic basis of those estimated parameters by applying standard QTL mapping methods, before feeding the QTL-based parameters back into the eco-physiological crop model, also produces satisfactory results. Yin *et al*. (2005) studied days to flowering in barley in this way. They modelled daily rate of progress towards flowering as a non-linear function of temperature and photoperiod and estimated 4 genotypic parameters from a photoperiod-controlled greenhouse experiment. These 4 genotypic input parameters were the minimum number of days to flowering at the optimum temperature and photoperiod, the development stage at the start of the photoperiod-sensitive phase, the development stage at the end of the photoperiod-sensitive phase, and the photoperiod sensitivity. The 4 genotypic input parameters of the eco-physiological model for days to flowering were subjected to a QTL analysis, with each physiological input parameter treated as a classical phenotypic response. From the QTL models fitted to the estimated physiological parameters, genotypic predictions were calculated and fed back into the non-linear eco-physiological model in the hope that these QTL-based input parameter values would lead to better predictions of the time to flowering than the 'phenotypic' parameters from the non-linear regressions. In formula form, the expectation for days to flowering for genotype i in environment j was $\mu_{ij} = f(x_{1i}(\rho_{1i}), x_{2i}(\rho_{2i}), x_{3i}(\rho_{3i}), x_{4i}(\rho_{4i}), z_{1j}, z_{2j})$, with f(.) the non-linear function producing the days to flowering from 4 genotypic input traits, x_1 to x_4, and 2 environmental covariables, daily temperature and photoperiod, z_1 and z_2. The parameter vectors ρ_{1i} to ρ_{4i} represent the QTL basis of the 4 genotypic input traits. A promising result of this study was that days to flowering in barley could indeed be well predicted from the QTL-based eco-physiological model, so that the combination of marker profile and environmental characterisation (daily temperature and photoperiod) sufficed for prediction of days to flowering for new genotypes in new environments.

Reymond *et al*. (2003) used a similar combination of eco-physiological modelling and QTL mapping for the prediction of GEI for leaf elongation rate in maize (see also Tardieu *et al*. 2005). The QTL analysis was performed on parameters of a linear model for predicting the leaf elongation rate as affected by meristem temperature, water vapour pressure difference, and soil water status. The combined QTL- and eco-physiological model successfully predicted leaf elongation rates for environments characterised by different climatic scenarios.

The 2-step approach to combined QTL-eco-physiological modelling can flexibly be extended to the study of more complex traits. Traits such as grain yield at the whole-crop level are the result of interactions among several physiological processes and their responses to environmental variables. Phenotypes such as development to flowering and leaf elongation rate are physiological components that underlie the formation of crop yield. Several researchers have emphasised the importance of dissecting a complex trait into its physiological components to identify QTLs that have a biological basis (Reymond *et al*. 2003; Hammer *et al*. 2005; Tardieu *et al*. 2005). A powerful tool for this dissection could be a crop-growth modelling framework, where simultaneous equations describing response curves of component processes to the environment are integrated according to crop physiological principles (Yin *et al*. 2004). Each component is then treated by the approach as outlined above for barley flowering time and maize leaf elongation rate. Yin *et al*. (2000) provided an example of such an exercise. They concluded that their crop growth models needed to be upgraded to achieve satisfactory resolution for dealing with complex traits. As a follow-up, Yin *et al*. (2004) discussed philosophy and methodology towards the development of such upgraded crop models, and recently Yin and van Laar (2005) introduced the GECROS model, an eco-physiological simulation model dedicated to the simulation of GEI. The inadequacy of earlier generations of crop growth models for addressing GEI was already acknowledged in the 1990s by a number of crop physiologists whose writings are included in the book by Cooper and Hammer (1996). These crop physiologists performed a general evaluation of multiple models and formulated recommendations for research, which since then has taken off (Hammer *et al*. 2005). Some key papers in this new tradition are Cooper *et al*. (2002*a*, 2002*b*) and Chapman *et al*. (2002, 2003).

A linkage disequilibrium approach to QTL mapping

The success of the approximate 2-step approaches to combined QTL-eco-physiological modelling of Reymond *et al*. (2003) and Yin *et al*. (2005), and the 1-step approaches discussed by Ma *et al*. (2002), Malosetti *et al*. (2004), and M. Malosetti and F. A. van Eeuwijk (unpublished data), shows that the methodology for the prediction of complex physiological responses in relation to genetic and environmental information has become sufficiently reliable to try its practical implementation in real-life breeding programs.

A point of concern may be that the present examples of combined QTL-eco-physiological modelling were all done on classical segregating populations from biparental crosses.

The question arises whether the results of such studies can be extrapolated to other crosses, i.e. other genetic backgrounds. An alternative to classical QTL studies with offspring from biparental crosses is linkage disequilibrium or association studies that look at linkage disequilibrium between markers and traits in diverse collections of genotypes. A point in favour of linkage disequilibrium studies is that they can be done on germplasm that represents a far wider genetic range than biparental offspring populations. On the negative side for linkage disequilibrium studies, there is the problem that linkage disequilibrium between markers and traits in diverse collections of genotypes does not necessarily follow from genetic linkage between marker and QTL. However, there are various ways to cope with that disadvantage. The work by Kraakman *et al*. (2004) illustrates the potential of a linkage disequilibrium approach for QTL-eco-physiological modelling. Danish variety trial yield data, spanning the period 1993–2000, on 146 modern 2-row spring barley cultivars, representing the current commercial germplasm in Europe, were used to estimate mean performance, adaptability (slopes of the regression on the mean model), and stability (variance around the regression on the mean line, Eqn 3). The cultivars were genotyped with 236 AFLP-markers, of which 123 were identified on an integrated map. Regression of the traits on individual marker data disclosed marker–trait associations for mean yield and yield stability. Many of the associated markers were located in regions where earlier QTLs were found for yield and yield components. To study the oligogenic base of the traits, multiple linear regression of the traits on markers was carried out using stepwise selection. By this procedure, 18–20 markers were selected to account for 40–58% of the variation in the studied complex traits. It was concluded that linkage disequilibrium approaches constitute a viable alternative to classical QTL approaches, especially for complex traits with costly measurements. As statistical models for linkage disequilibrium studies are very comparable with the models for classical QTL studies, the theoretical way forwards to the integration of QTL-modelling and eco-physiological modelling would seem to be the application of 1-step QTL-eco-physiological models in a linkage disequilibrium context, using diverse collections of genotypes that are known to exhibit interesting physiological contrasts on a phenotypic level.

Discussion

The treatment of the linear models in this paper was restricted to the modelling of the expected response, or mean, in its dependence on genotypic and environmental covariables, and little or no attention was given to variance-covariance aspects of the data. When we write the model for the phenotype of genotype i in environment j as $P_{ij} = \mu_{ij} + \varepsilon_{ij}$, where ε_{ij} is the error term, the statistical modelling for multi-environment trial data consists in first finding an adequate variance-covariance model for ε_{ij}, after which the search for a parsimonious model for μ_{ij} can start. The final choice of variance-covariance model can have important implications for the conclusions on the structure of the model for the mean. In the case of QTL modelling, QTLs may erroneously be declared significant or non-significant because of over/underestimation of effect sizes and standard errors (Malosetti *et al*. 2004; Piepho and Pillen 2004). Standard linear models assume that the error terms are independent and have constant variance. For the modelling of multi-environment trials, these assumptions are overly simplistic as variances and correlations tend to be heterogeneous across environments (Smith 1999; van Eeuwijk *et al*. 2001*a*). The mixed model framework, that combines modelling of mean and variance, provides a more appropriate modelling environment for GEI and QEI. Mixed models allow the investigation of the structure of the mean, including the genetic basis of complex traits in the form of sets of QTLs, while simultaneously offering flexibility with regard to assumptions on heterogeneity in residual (polygenic) variances and correlations across environments. Some examples of the application of mixed models to QTL mapping for multi-environment trials are Piepho (2000), Verbyla *et al*. (2003), Malosetti *et al*. (2004), and Piepho and Pillen (2004).

Linear models constitute the basic vehicle within quantitative genetics, but are often thought to be badly equipped for predictive gene-to-phenotype modelling of complex traits, where we think of a gene-to-phenotype model as a model that specifies trait performance by the outcome of the combined effect of a set of genes (Cooper *et al*. 2002*a*, 2002*b*, 2005). One reason for the inadequacy of linear models would be the supposed difficulties in mutually dealing with interactions between genes and between genes and environments (Cooper *et al*. 2005). Within a crop growth model such interactions will arise as an emergent property of the framework (Cooper *et al*. 2002*a*, 2002*b*; Yin *et al*. 2004; Hammer *et al*. 2005). Furthermore, the number of model terms to deal with such interactions in linear models would increase rapidly to impractical levels. In contrast, within gene-networks, interactions between genes form the default situation and additivity/linearity is the derived, more complex situation (Welch *et al*. 2005). It is true that within standard linear models the network-like relationships with feed-back loops that characterise crop growth models and gene networks do not have a natural counterpart. On the other hand, this paper contains examples that show how regression structures for GEI and QEI in linear models can closely mimic physiological responses if variable searches are initiated from sets of physiologically relevant genotypic and environmental covariables. For the composition of such sets of covariables the involvement of physiologists is essential. Linear models can be quite successful in the description of GEI and QEI when the modelling of interaction terms is based on physiological ‘control equations’ or

'meta-mechanisms'. Hammer *et al*. (2005) emphasise the importance of the quantification of the phenotypic response at a given time as a function of environmental inputs, i.e. control equations, to arrive at a dissection of the complex phenotype that produces intrinsically stable QTLs. Tardieu *et al*. (2005) see the legitimacy of meta-mechanisms, control equations at the plant level that make the plant respond in a predictable way to environmental changes, in their stability across environmental scenarios and their compatibility with physiological knowledge. Therefore, the statistical modelling of GEI and QEI should closely follow attempts at the definition of control equations and meta-mechanisms by physiologists. The advantage of placing such physiological knowledge within a statistical framework is that the powerful apparatus for inference that accompanies (mixed) linear models will be available for the exploration of the genetic base of complex traits in direct interaction with environmental triggers, growth factors, and limitations.

Gene × environment interactions thus seem amenable to satisfactory representation by (mixed) linear models. For the modelling of interactions between genes (QTLs), the number of parameters looks prohibitive for incorporation in linear models. However, by imposing penalties on the estimates for such interactions, genome screens on epistatic interactions become feasible (Boer *et al*. 2002). Such penalties can be translated into a mixed model framework, a topic that we are presently studying. Selection on epistatic interactions at a phenotypic level is hindered by the practical problems in obtaining reliable estimates of epistatic variances (Walsh 2005), but utilisation of epistatic interactions by construction of genotypes containing synergistic alleles at different QTLs should be within reach.

To develop an appreciation of the predictive power of some classical linear and bilinear models we have composed Table 2. In Table 2 we concentrate on the predictions of genotypic differences for environments that were not used in the estimation of the genotypic parameters that characterise the response to the environment. The only model that is devoid of any predictive power is the full interaction model since this model requires the estimation of parameters for each individual genotype × environment combination that is considered. Maybe somewhat surprisingly to many, the regression on the mean model, the AMMI model, and the factorial regression model with a genotypic covariable for GEI, all can produce predictions of genotypic differences for new environments as long as those new environments can somehow be identified as being similar to environments that were used in the fit of the model to the multi-environment data. This requirement emphasises the important role of environmental characterisation in the analysis and utilisation of knowledge of GEI and QEI. We acknowledge that in most cases the assessment of testing environments and new environments being similar contains a subjective element, but it is certainly not impossible. See Hammer *et al*. (2005) for an illustrative example of how this approach can be applied to study GEI and QEI. In addition to the just-mentioned models, a factorial regression model describing QEI can also be used for this coarse kind of prediction. The trick then consists in the decision of whether in the new environment a similar kind of QEI can be expected as in one of the test environments. Most credible are the predictive powers of factorial regression models including environmental covariables for GEI and QEI, especially when these statistical models are based on physiological control equations. In the last column of Table 2, it is indicated whether the model would classify as a gene-to-phenotype model. For this qualification to be positive, the model would need to bear a gene or QTL representation, and so only the last 3 models would classify.

Nevertheless, the difference between 'phenotypic' models for GEI and gene-to-phenotype models for QEI seems, especially within the context of statistical modelling, sooner gradual, i.e. representing a smooth transition, than essential,

Table 2. Expressions for genotypic differences in the evaluation environment *j*, according to different linear and bilinear models for the analysis of multi-environment trials, the possibility of predictions for a new environment *j, and the qualification of the models as gene-to-phenotype (GP) models**

AMMI, Additive main effects and multiplicative interaction; FR, factorial regression

Model[A]	Genotypic difference in env. *j*	Prediction for env. *j**	GP model
Additive (1)	$\{G_i - G_{i^*}\}$	Same as for env. *j*	No
Full interaction (2)	$\{G_i - G_{i^*}\} + \{(GE)_{ij} - (GE)_{i^*j}\}$	Impossible	No
Regression on the mean (3)	$\{G_i - G_{i^*}\} + \{(\beta_i - \beta_{i^*})E_j\}$	Only when env. *j* is similar to env. *j**	No
AMMI with 2 bilinear terms (4)	$\{G_i - G_{i^*}\} + \{(a_{1i} - a_{1i^*})b_{1j}\} + \{(a_{2i} - a_{2i^*})b_{2j}\}$	Only when env. *j* is similar to env. *j**	No
FR with environmental covariable (5)	$\{G_i - G_{i^*}\} + \{(\beta_i - \beta_{i^*})z_j\}$	Replace z_j by z_{j^*}	No
FR with genotypic covariable (6)	$\{G_i - G_{i^*}\} + \{(x_i - x_{i^*})\rho_j\}$	Only when env. *j* is similar to env. *j**	No
Single QTL with only main effect (7)	$\{(x_i - x_{i^*})\rho\}$	Same as for env. *j*	Yes
Single QTL with QEI (8)	$\{(x_i - x_{i^*})\rho\} + \{(x_i - x_{i^*})\rho_j\}$	Only when env. *j* is similar to env. *j**	Yes
Single QTL with QEI as regression on environmental covariable (9)	$\{(x_i - x_{i^*})\rho\} + \{\lambda(x_i - x_{i^*})z_j\}$	Replace z_j by z_{j^*}	Yes

[A]Number in parentheses is most appropriate equation number in text.

i.e. an abrupt difference. Linear models can cover a wide range of applications, including the modelling of the genetic basis of complex traits in relation to environmental factors. Gene × environment and genotype × environment interactions can be catered for in ways reminiscent of the incorporation of such interactions in crop growth models. Gene × gene and gene × genetic background interactions can be dealt with using penalties on parameter estimates thereby restraining the effective number of parameters. The largest challenges for statistical models lie in representations of networks and non-linear relations. However, the development of graphical models (for an overview see Edwards 2000), generalised linear (mixed) models, and non-linear mixed models (for an overview see Schabensberger and Pierce 2002) shows that there is no reason why gene-to-phenotype models could not be merely advanced statistical models.

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References

Boer MP, ter Braak CJF, Jansen RC (2002) A penalized likelihood method for mapping epistatic quantitative trait loci with one-dimensional genome searches. *Genetics* **162**, 951–960.

Chapman SC, Cooper M, Butler DG, Henzell RG (2000*a*) Genotype by environment interactions affecting grain sorghum. I. Characteristics that confound interpretation of hybrid yield. *Australian Journal of Agricultural Research* **51**, 197–207. doi: 10.1071/AR99020

Chapman SC, Cooper M, Hammer GL (2002) Using crop simulation to generate genotype by environment interaction effects for sorghum in water-limited environments. *Australian Journal of Agricultural Research* **53**, 379–389. doi: 10.1071/AR01070

Chapman SC, Cooper M, Hammer GL, Butler DG (2000*b*) Genotype by environment interactions affecting grain sorghum. II. Frequencies of different seasonal patterns of drought stress are related to location effects on hybrid yields. *Australian Journal of Agricultural Research* **51**, 209–221. doi: 10.1071/AR99021

Chapman SC, Cooper M, Podlich D, Hammer GL (2003) Evaluating plant breeding strategies by simulating gene action and dryland environment effects. *Agronomy Journal* **95**, 99–113.

Chapman SC, Hammer GL, Butler DG, Cooper M (2000*c*) Genotype by environment interactions affecting grain sorghum. III. Temporal sequences and spatial patterns in the target population of environments. *Australian Journal of Agricultural Research* **51**, 223–233. doi: 10.1071/AR99022

Comstock RE (1977) Quantitative genetics and the design of breeding programs. In 'Proceedings of the International Conference on Quantitative Genetics'. 16–21 August 1976. pp. 705–718. (Iowa State University Press: Ames, IA)

Cooper M, Chapman SC, Podlich DW, Hammer GL (2002*a*) The GP problem: Quantifying gene-to-phenotype relationships. *In Silico Biology* **2**, 151–164.

Cooper M, Hammer GL (Eds) (1996) 'Plant adaptation and crop improvement.' (CAB International: Wallingford, UK)

Cooper M, Podlich DW, Micallef KP, Smith OS, Jensen NM, Chapman SC, Kruger NL (2002) Complexity, quantitative traits and plant breeding: a role for simulation modelling in the genetic improvement of crops. In 'Quantitative genetics, genomics and plant breeding'. (Ed. MS Kang) pp. 143–166. (CAB International: Wallingford, UK)

Cooper M, Podlich DW, Smith OS (2005) Gene-to-phenotype models and complex trait genetics. *Australian Journal of Agricultural Research* **56**, 895–918.

Crossa J, Cornelius P (2002) Linear–bilinear models for the analysis of genotype–environment interaction. In 'Quantitative genetics, genomics and plant breeding'. (Ed. MS Kang) pp. 305–322. (CAB International: Wallingford, UK)

Denis J-B (1988) Two-way analysis using covariates. *Statistics* **19**, 123–132.

Denis J-B, Gower JC (1996) Asymptotic confidence regions for biadditive models: interpreting genotype-environment interactions. *Applied Statistics* **45**, 479–492.

Edwards D (2000) 'Introduction to graphical modelling.' (Springer: New York)

van Eeuwijk FA (1995*a*) Linear and bilinear models for the analysis of multi-environment trials: I An inventory of models. *Euphytica* **84**, 1–7. doi: 10.1007/BF01677551

van Eeuwijk FA (1995*b*) Multiplicative interaction in generalized linear models. *Biometrics* **51**, 1017–1032.

van Eeuwijk FA, Cooper M, DeLacy IH, Ceccarelli S, Grando S (2001*a*) Some vocabulary and grammar for the analysis of multi-environment trials, as applied to the analysis of FPB and PPB trials. *Euphytica* **122**, 477–490. doi: 10.1023/A:1017591407285

van Eeuwijk FA, Crossa J, Vargas M, Ribaut JM (2001*b*) Variants of factorial regression for analysing QTL by environment interaction. In 'Eucarpia, quantitative genetics and breeding methods: the way ahead'. Les colloques series 96. (Eds A Gallais, C Dillmann, I Goldringer) pp. 107–116. (INRA Editions: Versailles, France)

van Eeuwijk FA, Crossa J, Vargas M, Ribaut J-M (2002) Analysing QTL by environment interaction by factorial regression, with an application to the CIMMYT drought and low nitrogen stress programme in maize. In 'Quantitative genetics, genomics and plant breeding'. (Ed. MS Kang) pp. 245–256. (CAB International: Wallingford, UK)

van Eeuwijk FA, Denis J-B, Kang MS (1996) Incorporating additional information on genotypes and environments in models for two-way genotype by environment tables. In 'Genotype-by-environment interaction'. (Eds MS Kang, HG Gauch) pp. 15–50. (CRC Press: Boca Raton, FL)

Finlay KW, Wilkinson GN (1963) The analysis of adaptation in a plant breeding programme. *Australian Journal of Agricultural Research* **14**, 742–754. doi: 10.1071/AR9630742

Gabriel KR (1978) Least squares approximation of matrices by additive and multiplicative models. *Journal of the Royal Statistical Society: Series B* **40**, 186–196.

Gabriel KR (1998) Generalised bilinear regression. *Biometrika* **85**, 689–700. doi: 10.1093/biomet/85.3.689

Gabriel KR, Zamir S (1979) Lower rank approximations of matrices by least squares with any choice of weights. *Technometrics* **21**, 489–498.

Gauch HG (1988) Model selection and validation for yield trials with interaction. *Biometrics* **44**, 705–715.

Gollob HF (1968) A statistical model which combines features of factor analysis and analysis of variance techniques. *Psychometrika* **33**, 73–115.

Haley CS, Knott SA (1992) A simple regression method for mapping quantitative trait loci in line crosses using flanking markers. *Heredity* **69**, 315–324.

Hammer GL, Chapman SC, van Oosterom E, Podlich DW (2005) Trait physiology and crop modelling as a framework to link phenotypic complexity to underlying genetic systems. *Australian Journal of Agricultural Research* **56**, 947–960.

Jiang C, Zeng Z-B (1997) Mapping quantitative trait loci with dominant and missing markers in various crosses from two inbred lines. *Genetica* **101**, 47–58. doi: 10.1023/A:1018394410659

Kraakman ATW, Niks RE, van den Berg PMMM, Stam P, van Eeuwijk FA (2004) Linkage disequilibrium mapping of yield and yield stability in modern spring barley cultivars. *Genetics* **168**, 435–446. doi: 10.1534/genetics.104.026831

Lynch M, Walsh JB (1998) 'Genetics and analysis of quantitative traits.' (Sinauer Associates: Sunderland, MA)

Ma CX, Casella G, Wu R (2002) Functional mapping of quantitative trait loci underlying the character process: a theoretical framework. *Genetics* **161**, 1751–1762.

Malosetti M, Voltas J, Romagosa I, Ullrich SE, van Eeuwijk FA (2004) Mixed models including environmental variables for studying QTL by environment interaction. *Euphytica* **137**, 139–145. doi: 10.1023/B:EUPH.0000040511.46388.ef

Mandel J (1969) The partitioning of interaction in analysis of variance. *Journal of Research – National Bureau of Standards, Mathematical Sciences* **73B**, 309–328.

Piepho HP (2000) A mixed model approach to mapping quantitative trait loci in barley on the basis of multiple environment data. *Genetics* **156**, 2043–2050.

Piepho HP, Pillen K (2004) Mixed modelling for QTL × environment interaction analysis. *Euphytica* **137**, 147–153. doi: 10.1023/B:EUPH.0000040512.84025.16

Reymond M, Muller B, Leonardi A, Charcosset A, Tardieu F (2003) Combining QTL analysis and an ecophysiological model to analyse the genetic variability of the responses of maize leaf growth to temperature and water deficit. *Plant Physiology* **131**, 664–675. doi: 10.1104/pp.013839

Schabensberger O, Pierce FJ (2002) 'Contemporary statistical models for the plant and soil sciences.' (CRC Press: Boca Raton, FL)

Smith AB (1999) Multiplicative mixed models for the analysis of multi-environment trial data. PhD thesis, Dept of Statistics, University of Adelaide, South Australia.

Tardieu F, Reymond M, Muller B, Granier C, Simonneau T, Sadok W, Welcker C (2005) Linking physiological and genetic analyses of the control of leaf growth under changing environmental conditions. *Australian Journal of Agricultural Research* **56**, 937–946.

Vargas M, Crossa J, van Eeuwijk FA, Ramírez ME, Sayre K (1999) Using AMMI, factorial regression, and partial least squares regression models for interpreting genotype × environment interaction. *Crop Science* **39**, 955–967.

Verbyla AP, Eckermann PJ, Thompson R, Cullis B (2003) The analysis of quantitative trait loci in multi-environment trials using a multiplicative mixed model. *Australian Journal of Agricultural Research* **54**, 1395–1408. doi: 10.1071/AR02239

Voltas J, van Eeuwijk FA, Araus JL, Romagosa I (1999*b*) Integrating statistical and ecophysiological analysis of genotype by environment interaction for grain filling of barley in Mediterranean areas II. Grain growth. *Field Crops Research* **62**, 75–84. doi: 10.1016/S0378-4290(99)00007-6

Voltas J, van Eeuwijk FA, Sombrero A, Lafarga A, Igartua E, Romagosa I (1999*a*) Integrating statistical and ecophysiological analysis of genotype by environment interaction for grain filling of barley in Mediterranean areas I. Individual grain weight. *Field Crops Research* **62**, 63–74. doi: 10.1016/S0378-4290(99)00006-4

Walsh B (2005) The struggle to exploit non-additive variation. *Australian Journal of Agricultural Research* **56**, 873–881.

Welch SM, Dong Z, Roe JL, Das S (2005) Flowering time control: gene network modelling and the link to quantitative genetics. *Australian Journal of Agricultural Research* **56**, 919–936.

Wu W, Zhou Y, Li W, Mao D, Chen Q (2002) Mapping of quantitative trait loci based on growth models. *Theoretical and Applied Genetics* **105**, 1043–1049. doi: 10.1007/s00122-002-1052-8

Yin X, Chasalow S, Dourleijn CJ, Stam P, Kropff MJ (2000) Coupling estimated effects of QTLs for physiological traits to a crop growth model: predicting yield variation among recombinant inbred lines in barley. *Heredity* **85**, 539–549. doi: 10.1046/j.1365-2540.2000.00790.x

Yin X, van Laar HH (2005) 'Crop systems dynamics. An ecophysiological simulation model for genotype-by-environment interactions.' (Wageningen Academic Publishers: The Netherlands)

Yin X, Struik PC, van Eeuwijk FA, Stam P, Tang J (2005) QTL analysis and QTL-based prediction of flowering phenology in recombinant inbred lines of barley. *Journal of Experimental Botany* **56**, 967–976. doi: 10.1093/jxb/eri090

Yin X, Struik PC, Kropff MJ (2004) Role of crop physiology in predicting gene-to-phenotype relationships. *Trends in Plant Science* **9**, 426–432. doi: 10.1016/j.tplants.2004.07.007

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