Increased Prediction Accuracy in Wheat Breeding Trials Using a Marker × Environment Interaction Genomic Selection Model

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ABSTRACT Genomic selection (GS) models use genome-wide genetic information to predict genetic values of candidates of selection. Originally, these models were developed without considering genotype × environment interaction (GxE). Several authors have proposed extensions of the single-environment GS model that accommodate GxE using either covariance functions or environmental covariates. In this study, we model GxE using a marker × environment interaction (MxE) GS model; the approach is conceptually simple and can be implemented with existing GS software. We discuss how the model can be implemented by using an explicit regression of phenotypes on markers or using co-variance structures (a genomic best linear unbiased prediction-type model). We used the MxE model to analyze three CIMMYT wheat data sets (W1, W2, and W3), where more than 1000 lines were genotyped using genotyping-by-sequencing and evaluated at CIMMYT’s research station in Ciudad Obregon, Mexico, under simulated environmental conditions that covered different irrigation levels, sowing dates and planting systems. We compared the MxE model with a stratified (i.e., within-environment) analysis and with a standard (across-environment) GS model that assumes that effects are constant across environments (i.e., ignoring GxE). The prediction accuracy of the MxE model was substantially greater of that of an across-environment analysis that ignores GxE. Depending on the prediction problem, the MxE model had either similar or greater levels of prediction accuracy than the stratified analyses. The MxE model decomposes marker effects and genomic values into components that are stable across environments (main effects) and others that are environment-specific (interactions). Therefore, in principle, the interaction model could shed light over which variants have effects that are stable across environments and which ones are responsible for GxE. The data set and the scripts required to reproduce the analysis are publicly available as Supporting Information.

The presence of genotype × environment (GxE) interactions in agricultural experiments usually is expressed as changes in the relative performance of genetic materials across environments; this can manifest as modifications of the ranking of genotypes across environments or simply as changes in the absolute difference in performance between pairs of genotypes. Accounting for GxE has always been a concern in the analysis of multi-environment plant breeding trials, and several models have been proposed and used for describing the mean response of genotypes over environments and for studying and interpreting GxE in agricultural experiments (e.g., Yates and Cochran 1938; Finlay and Wilkinson, 1963; Eberhart and Russell 1966).

The statistical treatment of GxE has evolved over time due to the development of statistical methods and because of changes in the information available, including the increased availability of DNA markers and of precise environmental information. Some approaches deal with GxE implicitly, without explicitly modeling gene × environment interactions; these include some of the early treatment of GxE (e.g., the joint-regression analysis of Yates and Cochran 1938), as well as more
modern methods such as the multivariate pedigree- or marker-based models where GxE is modeled using structured or unstructured covariance functions (Piepho, 1997, 1998; Smith et al. 2005; Crossa et al. 2006; Burgueño et al. 2007). These approaches have proved to be effective for exploiting GxE; however, they do not shed light on the underlying basis of GxE (e.g., the relative contribution of different genetic regions to stability and to GxE). When genomic and environmental covariate data are available, GxE can be modeled explicitly by means of marker x environment interactions (MxE). This approach was first used with sparse marker data in quantitative trait loci (QTL) analysis (QTLxE Moreau et al. 2004) and also in multifocus models with markers that exhibited “significant” association with the trait of interest (Boer et al. 2007). The QTLxE approach has been further extended to multitrait, multienvironment settings (e.g., Malosetti et al. 2004, 2008).

Recent developments in genotyping and sequencing technologies have made it possible to use dense genotypic information for genomic selection (GS) (Meuwissen et al. 2001). Empirical evidence obtained with plant and animal breeding data has demonstrated that GS can outperform the prediction accuracy of pedigree-based methods or that with plant and animal breeding data has demonstrated that GS can accommodate GxE (e.g., Malosetti et al. 2004, 2008). More recently, Heslot et al. (2014) considered modeling GxE using both genetic markers and environmental covariates. These studies also showed that modeling GxE can give substantial gains in prediction accuracy.

Following ideas originally used for QTL analysis in multienvironment trials (Van Eeuwijk et al. 2005; Boer et al. 2007; Malosetti et al. 2004, 2008), we present GS models that accommodate GxE by explicitly modeling interactions between all available markers and environments. Relative to multivariate approaches where GxE is modeled using covariance parameters (e.g., Smith et al. 2005), the MxE approach has advantages and disadvantages. First, the MxE models presented here can be easily implemented using existing software for GS. Second, the model can be implemented using both shrinkage methods as well as variable selection methods. Third, the MxE model decomposes effects into components that are common across environments (stability) and environment-specific deviations; this information, which is not provided by standard multienvironment mixed models, can be used to identify genomic regions whose effects are stable across environments and others that are responsible for GxE. On the other hand, the MxE model imposes restrictions on the patterns of GxE, and, for reasons that we discuss in this article, the model is best suited for the joint analysis of positively correlated environments.

In this study, we applied the MxE model to extensive data sets where wheat lines were evaluated under contrasting environmental conditions in replicated field trials. This allowed us to identify under which conditions the MxE model is most effective. We show theoretically and demonstrate empirically that the magnitude of the main and interaction variance is directly related to the phenotypic correlation between environments and that the MxE model performs best when the set of environments analyzed showed positive and similar correlations. Indeed, when the set of environments analyzed had moderate or high positive correlations, the MxE model yielded substantial gains in prediction accuracy relative to an across-environment GS model that assumes homogeneity of effects across environments, and, depending on the prediction problem, it either performed similarly or outperformed the stratified (i.e., within-environment) analyses. In the rest of this article, we describe the methods used and present empirical results obtained when the MxE model was applied to three wheat data sets. We also provide, as online materials, scripts that implement the interaction models using the BGLR R-package (de los Campos and Pérez-Rodríguez 2014).

**MATERIALS AND METHODS**

The data used in this study are from CIMMYT’s Global Wheat Program and consist of a set of wheat lines evaluated under managed environmental conditions; these conditions were designed to simulate target mega-environments. The wheat lines included in this study were later part of the 45th, 46th, and 47th International Bread Wheat Screening Nurseries and distributed worldwide.

Three files containing phenotypic and genotypic information on the three data sets used in this study (45th, 46th and 47th International Bread Wheat Screening Nurseries) are provided as Supporting Information, File S1, File S2, and File S3, respectively.

**Phenotypic data**

The phenotypic data consisted of adjusted grain yield (ton/ha) records collected during three evaluation cycles (W1: cycle 2010–2011, N = 732; W2: cycle 2011–2012, N = 672; and W3: cycle 2012–2013, N = 811); each cycle included a different set of advanced breeding lines. All trials were established at CIMMYT’s main wheat breeding station at Cd. Obregon, Mexico. The experimental design was an alpha-lattice with three replicates per line and environment. Wheat lines were evaluated under three irrigation regimes (2i = two irrigations giving moderate drought stress, 5i = five irrigations representing an optimally irrigated crop, and 0i = no irrigation or drip irrigation, representing high drought stress), two planting systems (B = bed planting; F = planting on the flat) and two planting dates (N = normal and H = late, simulating heat at the grain-filling stage). In the 2i and 5i regimes, irrigation was applied without measuring soil moisture, and each irrigation added 100 mm of water. Some of the trials were managed using no-tillage (hereinafter denoted as Z). Table 1 gives the number of phenotypic records per simulated environment and cycle. The phenotype used in the analysis was the best linear unbiased estimate of grain yield obtained from a linear model applied to the alpha-lattice design of each cycle-environment combination.

**Genotypic data**

Genotypes were derived using genotyping-by-sequencing technology (GBS; Poland et al. 2012). GBS markers with a minor allele frequency lower than 0.05 were removed. As is typical of GBS genotypes, all markers had a high incidence of uncalled genotypes. In our quality control pipeline, we applied thresholds for incidence of missing values aimed at maintaining relatively large and similar numbers of markers per data set. To this end, we removed markers with more than 60% (W1 and W2) or 80% (W3) missing values; this left 15,744 (W1 and W2) or 14,217 (W3) GBS markers available for analysis. Finally, only lines with more than 2000 called GBS markers were used in the data analysis; this left 693 (W1), 670 (W2), and 807 (W3) lines.

**Statistical models**

For each evaluation cycle (W1, W2, and W3), we considered three approaches: (i) a stratified analysis obtained by regressing phenotypes on markers separately in each environment (we refer to this approach, indistinctively, as to single-environment, within-environment or
Stratified analysis: This model is obtained by regressing the phenotype vector containing the records available in the $j$th environment, $y_j = \{y_{ij}\}$, where $i$ indexes lines (individuals) and $j$ indexes environments, on markers using a linear model in the form: $y_{ij} = \mu + \sum_{k=1}^p x_{ijk} \beta_k + e_{ij}$, $i = 1,2,\ldots,n$ individuals; $j = 1,2,\ldots,s$ environments; $k = 1,2,\ldots,p$ markers) or, in matrix notation,

$$y_j = 1 \mu_j + X \beta_j + e_j \quad (1a)$$

where $\mu_j$ is an intercept, $X_j = \{x_{ijk}\}$ is a matrix of marker-centered and standardized genotypes (i.e., each marker was centered by subtracting the mean and standardized by dividing by the sample standard deviation), $\beta_j = \{\beta_k\}$ is a vector of marker effects and $e_j$ is a vector of model residuals. Note that, in a full-factorial design where all lines are evaluated in all environments, $X_1 = X_2 = \ldots = X_p$. Following the standard assumptions of the GBLUP model (e.g., Vanraden, 2007, 2008), marker effects and model residuals were assumed to be independent of each other and both normally distributed: $\beta_j \sim N(0, \text{I} \sigma^2_{\beta})$, and $e_j \sim N(0, \text{I} \sigma^2_e)$. Setting $u_j = X \beta_j$, we have that the aforementioned model also can be represented as follows:

$$y_j = 1 \mu_j + u_j + e_j \quad (1b)$$

with $u_j \sim N(0, G_0 \sigma^2_{\beta})$, where $G_0 = \frac{XX'}{p}$ was obtained using the cross-product of (centered and standardized) marker genotypes and scaled by dividing by the number of markers. Because all markers were standardized to a unit variance, this gives an average diagonal value of $G_0$ equal to one.

Box 1a in File S4 provides an R-script that implements the single-environment model described previously using the BGLR R-package (de los Campos and Pérez-Rodriguez 2014).

Across-environment GBLUP model: another approach consists of assuming that effects of markers are the same across environments, that is: $\beta_1 = \beta_2 = \ldots = \beta_s = \beta$; therefore the regression model (1b) becomes (assuming $s = 3$, for ease of notation):

$$\begin{bmatrix} y_1 \\ y_2 \\ y_3 \end{bmatrix} = \begin{bmatrix} 1 & \mu_1 \\ 1 & \mu_2 \\ 1 & \mu_3 \end{bmatrix} + \begin{bmatrix} X_1 \\ X_2 \\ X_3 \end{bmatrix} \beta + \begin{bmatrix} e_1 \\ e_2 \\ e_3 \end{bmatrix} \quad (2a)$$

In a GBLUP-context, one will assume $\beta \sim N(0, \text{I} \sigma^2_{\beta})$ and the aforementioned model can be represented as a random effect model as follows:

$$\begin{bmatrix} y_1 \\ y_2 \\ y_3 \end{bmatrix} = \begin{bmatrix} 1 & \mu_1 \\ 1 & \mu_2 \\ 1 & \mu_3 \end{bmatrix} + \begin{bmatrix} u_1 \\ u_2 \\ u_3 \end{bmatrix} + \begin{bmatrix} e_1 \\ e_2 \\ e_3 \end{bmatrix} \quad (2b)$$

where $u_j = X \beta$, and $u = (u_1' + u_2' + u_3')' \sim N(0, G_0 \sigma^2_{\beta})$, where $G_0 = \frac{XX}{p}$ is a marker-derived genomic relationship matrix. It is worth noting that, for balanced data, the model of expression (2a) is equivalent to fitting a genomic regression model using the average performance of each line across environments as a phenotype.

Box 2a in File S4 provides an R-script that implements the across-environment model described above using the BGLR R-package (de los Campos and Pérez-Rodriguez 2014).

**MxE GBLUP model:** In the model in expression (1a), marker effects ($\beta$) are estimated separately for each environment; therefore, in this model there is no borrowing of information across environments. On the other hand, in the model in expression (2a), all data are used to estimate marker effects; however, in that model borrowing of information is achieved by assuming that effects are constant across environments. We now consider an interaction model that aims at benefiting from borrowing information across environments while allowing marker effects to change across environments. In the MxE model, the effect of the $k$th marker on the $j$th environment ($\beta_{kj}$) is described as the sum of an effect common to all environments ($b_{jk}$), plus a random deviation ($b_{jk}$) peculiar to the $j$th environment, that is $\beta_{kj} = b_{jk} + b_{jk}$. Therefore, the equation for data from the $j$th environment becomes:

$$y_j = 1 \mu_j + u_j + e_j$$

with $u_j \sim N(0, G_0 \sigma^2_{\beta})$, where $G_0 = \frac{XX}{p}$ was obtained using the cross-product of (centered and standardized) marker genotypes and scaled by dividing by the number of markers. Because all markers were standardized to a unit variance, this gives an average diagonal value of $G_0$ equal to one.

**Table 1 Number of phenotypic records per cycle (W1, W2, and W3) and environment**

| Environment* | Data Set |
|--------------|----------|
|              | W1 (Cycle 2010-11, 45th IBWSN) | W2 (Cycle 2011-12, 46th IBWSN) | W3 (Cycle 2012-13, 47th IBWSN) |
| 0iBN         | 693      | –   | –   |
| 0iFN         | –        | 670 | 807 |
| 2iBN         | 693      | –   | 807 |
| 5iBNZ        | 693      | –   | –   |
| 5iBH         | –        | 670 | 807 |
| 5iBN         | –        | 670 | 807 |
| 5iFN         | 693      | 670 | 807 |
| Total        | 2772     | 2680| 4035|

* Environments are described by a sequence of codes: 0, 2, and 5 denote the number of irrigation cycles; B/F denotes whether the planting system was ‘bed’ (B) or ‘flat’ (F); N/H denotes whether planting date was normal (N) or late (H, simulating heat); Z indicates no tillage. IBWSN denotes International Bread Wheat Screening Nurseries.
environment becomes \( y_{ij} = \mu + \sum_{k=1}^{p} x_{ik} (b_k + b_{ij} + \varepsilon_{ij}) \), or, in matrix notation and assuming, for ease of notation, only three environments,

\[
\begin{bmatrix}
y_1 \\
y_2 \\
y_3
\end{bmatrix} = \begin{bmatrix} 1 & 1 & 1 \\ 1 & 1 & 1 \\ 1 & 1 & 1 \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_2 \\ \mu_3 \end{bmatrix} + \begin{bmatrix} X_1 \\ X_2 \\ X_3 \end{bmatrix} \begin{bmatrix} b_1 \\ b_2 \\ b_3 \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \varepsilon_3 \end{bmatrix},
\]

where the vectors of main and interaction effects and model residuals were all assumed to be normally distributed, specifically:

\( b_0 \sim N(0, \sigma^2_{b0}), b_i \sim N(0, \sigma^2_{bi}) \) and \( \varepsilon_i \sim N(0, \sigma^2_{\varepsilon}) \). The aforementioned model can be represented as a two-variance component GBLUP model, specifically, letting \( y = (y_1', y_2', y_3')' \),

\[
\begin{align*}
\mu &= \begin{bmatrix} \mu_1 \\ \mu_2 \\ \mu_3 \end{bmatrix}, u_0 = \begin{bmatrix} X_1 \\ X_2 \\ X_3 \end{bmatrix} b_0, u_1 = \begin{bmatrix} X_1 & 0 & 0 \\ 0 & X_2 & 0 \\ 0 & 0 & X_3 \end{bmatrix} b_1 \\
\end{align*}
\]

the model can be represented as

\[
y = \mu + u_0 + u_1 + \varepsilon,
\]

where \( u_0 \sim N(0, \sigma^2_{u0}), u_1 \sim N(0, G_1), \varepsilon \sim N(0, \sigma^2_{\varepsilon}) \) where \( G_0 \) is as described previously and

\[
G_1 = \begin{bmatrix} \sigma^2_{u0} X_1 X_1' & 0 & 0 \\ 0 & \sigma^2_{u1} X_2 X_2' & 0 \\ 0 & 0 & \sigma^2_{\varepsilon} X_3 X_3' \end{bmatrix} / p
\]

### Table 2 SD (diagonal) and sample correlation (lower-triangular) between grain yields evaluated under different environmental conditions, by cycle

|          | 0iBN | 2iBN | 5iBNZ | 5iFN |
|----------|------|------|-------|------|
| **W1 (cycle 2010-2011, 45th IBWSN)** |      |      |       |      |
| Environment * |      |      |       |      |
| 0iBN     | 0.61 |      |       |      |
| 2iBN     | 0.53 (0.47-0.58) | 0.51 |
| 5iBNZ    | 0.25 (0.18-0.32) | 0.34 (0.27-0.40) | 0.60 |
| 5iFN     | 0.26 (0.19-0.33) | 0.33 (0.26-0.39) | 0.22 (0.15-0.29) | 0.63 |
| **W2 (cycle 2011-2012, 46th IBWSN)** |      |      |       |      |
| Environment |      |      |       |      |
| 0iFN     | 0.54 |      |       |      |
| 5iBN     | 0.34 (0.27-0.41) | 0.60 |
| 5iBN     | -0.05 (-0.13,0.02) | 0.33 (0.26,0.39) | 0.65 |
| 5iFN     | 0.31 (0.24-0.38) | 0.41 (0.35,0.47) | 0.41 (0.35-0.47) | 0.58 |
| **W3 (cycle 2012-2013, 47th IBWSN)** |      |      |       |      |
| Environment |      |      |       |      |
| 0iFN     | 0.51 |      |       |      |
| 2iBN     | 0.17 (0.10-0.23) | 0.41 |
| 5iBN     | 0.30 (0.24-0.36) | -0.03 (-0.10,0.04) | 0.60 |
| 5iFN     | -0.10 (-0.16, -0.03) | 0.12 (0.05-0.19) | -0.09 (-0.16, -0.02) | 0.49 |
| 5iFN     | -0.01 (-0.08,0.06) | 0.04 (-0.03,0.10) | 0.02 (-0.05,0.09) | 0.55 (0.50-0.59) | 0.51 |

95% confidence interval for the correlations are given in parentheses. IBWSN, International Bread Wheat Screening Nurseries *Environments are described by a sequence of codes: 0i, 2i, and 5i denote the number of irrigation cycles; B/F denotes whether the planting system was “bed” (B) or “flat” (F); N/H denotes whether planting date was normal (N) or late (H, simulating heat); Z indicates no tillage.
In this model, the main effect ($u_0$) allows borrowing information between environments (through the off-diagonal blocks of $G_0$) and $u_1$ captures environment-specific effects. The relative importance of these two terms is determined by the corresponding variance components that are inferred from the data.

### Table 3 Estimates of variance components (estimated posterior SD) by model and environment, cycle 2010–2011 (W1)

| Models/Environments | Residual | Main Effect | Interaction (MxE) | R-Squared$^b$ |
|---------------------|----------|-------------|------------------|---------------|
| **Single environment** |          |             |                  |               |
| 0iBN                | 0.529(0.037) | 0.400(0.066) | –                | 0.429(0.049)  |
| 2iBN                | 0.362(0.031) | 0.609(0.082) | –                | 0.624(0.044)  |
| 5iBNZ               | 0.549(0.043) | 0.533(0.089) | –                | 0.489(0.053)  |
| 5iFN                | 0.584(0.041) | 0.370(0.064) | –                | 0.386(0.050)  |
| **Pairs of environments** |          |             |                  |               |
| 0iBN                 | 0.429(0.022) | 0.497(0.023) | 0.427(0.057) | 0.433(0.054) | 0.092(0.031) | 0.545(0.036) | 0.464(0.036) |
| 2iBN                 | 0.527(0.029) | 0.714(0.032) | 0.188(0.054) | 0.239(0.042) | 0.220(0.061) | 0.433(0.046) | 0.250(0.036) |
| 5iBNZ                | 0.558(0.028) | 0.681(0.029) | 0.173(0.045) | 0.228(0.037) | 0.198(0.055) | 0.396(0.044) | 0.250(0.033) |
| 0iBN                 | 0.434(0.025) | 0.609(0.028) | 0.367(0.062) | 0.374(0.052) | 0.202(0.059) | 0.564(0.039) | 0.379(0.037) |
| 5iBNZ                | 0.474(0.026) | 0.634(0.028) | 0.254(0.052) | 0.290(0.042) | 0.252(0.061) | 0.513(0.041) | 0.313(0.034) |
| 0iBN                 | 0.577(0.031) | 0.723(0.031) | 0.134(0.046) | 0.221(0.037) | 0.351(0.084) | 0.453(0.049) | 0.234(0.032) |
| 5iFN                 | 0.485(0.018) | 0.681(0.020) | 0.316(0.042) | 0.272(0.034) | 0.116(0.038) | 0.472(0.035) | 0.285(0.027) |

$^a$ Environments are described by a sequence of codes: 0i, 2i, and 5i denote the number of irrigation cycles; B/F denotes whether the planting system was “bed” (B) or “flat” (F); N/H denotes whether planting date was normal (N) or late (H, simulating heat); Z indicates no tillage.

$^b$ Model $R^2$ was computed as the ratio of the sum of the main and interaction variance, relative to the total variance (residual + main effect + interaction). Env, environment.

In this model, the main effect ($u_0$) allows borrowing information between environments (through the off-diagonal blocks of $G_0$) and $u_1$ captures environment-specific effects. The relative importance of these two terms is determined by the corresponding variance components that are inferred from the data.

### Table 4 Estimates of variance components (estimated posterior SD) by model and environment, cycle 2011–2012 (W2)

| Models/Environments | Residual | Main Effect | Interaction (MxE) | R-Squared$^b$ |
|---------------------|----------|-------------|------------------|---------------|
| **Single environment** |          |             |                  |               |
| 0iFN                | 0.563(0.046) | 0.512(0.099) | –                | 0.473(0.060)  |
| 5iBH                | 0.606(0.046) | 0.488(0.088) | –                | 0.443(0.055)  |
| 5iBN                | 0.492(0.041) | 0.612(0.097) | –                | 0.551(0.052)  |
| 5iFN                | 0.611(0.046) | 0.423(0.080) | –                | 0.407(0.055)  |
| **Pairs of environments** |          |             |                  |               |
| 0iFN                 | 0.541(0.032) | 0.712(0.034) | 0.371(0.079) | 0.344(0.060) | 0.223(0.073) | 0.520(0.051) | 0.325(0.043) |
| 5iBH                 | 0.532(0.032) | 0.841(0.036) | 0.056(0.023) | 0.149(0.029) | 0.476(0.096) | 0.495(0.053) | 0.151(0.026) |
| 5iBN                 | 0.532(0.031) | 0.729(0.035) | 0.389(0.082) | 0.324(0.058) | 0.232(0.071) | 0.535(0.050) | 0.307(0.042) |
| 5iFN                 | 0.537(0.029) | 0.668(0.031) | 0.370(0.065) | 0.388(0.057) | 0.184(0.062) | 0.505(0.044) | 0.367(0.039) |
| 5iBN                 | 0.533(0.030) | 0.651(0.032) | 0.441(0.075) | 0.428(0.067) | 0.147(0.050) | 0.513(0.044) | 0.396(0.042) |
| 5iFN                 | 0.539(0.029) | 0.617(0.030) | 0.381(0.065) | 0.407(0.059) | 0.169(0.058) | 0.502(0.044) | 0.396(0.040) |
| **All environments** |          |             |                  |               |
| 0iFN                | 0.519(0.021) | 0.737(0.022) | 0.436(0.056) | 0.334(0.045) | 0.400(0.076) | 0.614(0.034) | 0.311(0.031) |
| 5iBH                | 0.147(0.046) | 0.528(0.036) | –                | 0.444(0.055)  |
| 5iFN                | 0.266(0.069) | 0.572(0.037) | –                | 0.450(0.055)  |
| 5iFN                | 0.097(0.033) | 0.504(0.034) | –                | 0.463(0.055)  |

$^a$ Environments are described by a sequence of codes: 0i, 2i, and 5i denote the number of irrigation cycles; B/F denotes whether the planting system was “bed” (B) or “flat” (F); N/H denotes whether planting date was normal (N) or late (H, simulating heat); Z indicates no tillage.

$^b$ Model $R^2$ was computed as the ratio of the sum of the main and interaction variance, relative to the total variance (residual + main effect + interaction).
Further details are given in de los Campos and Pérez-Rodriguez (2014). We used a Bayesian model assuming Gaussian priors for the marker effects. The BGLR package assigns scaled-inverse χ² densities to the variance parameters whose hyperparameters were given values using the default rules implemented in BGLR, which assign 5 degrees of freedom and calculates the scale parameter based on the sample variance of the phenotypes. Further details are given in de los Campos and Pérez-Rodriguez (2014).

### Statistical analysis

The aforementioned models were fitted to data from each of the cycles (W1–W3), separately. For each cycle data we performed analysis: (i) within-environment (see expression 1a), or (ii) by pairs of environments or, (iii) using data from all environments together. These last two approaches were implemented either using the model in expression (2a) or the interaction model expression (3a).

Models were fitted to each of the full data sets to derive estimates of variance components. Subsequently, we assessed prediction accuracy using training-testing (i.e., TRN-TST) random partitions (see below). For this validation procedure, all the parameters of the models, including variance components, were re-estimated from TRN data in each of the TRN-TST partitions. In all cases, inferences and predictions were based on 55,000 samples collected from the posterior distribution after discarding 5000 samples for burn-in.

Prediction accuracy was assessed using 50 TRN-TST random partitions; we used this approach because with a replicated TRN-TST design one can obtain as many partitions as one needs and this allows estimating SEs of estimates of prediction accuracy more precisely than with a cross-validation approach. Following Burgueño et al. (2012), we considered two different prediction problems. First (CV1), we assessed prediction accuracy of the models when TRN and TST data consist of disjoint sets of lines; this approach mimics the prediction problem.
faced by breeders when lines have not been evaluated in any field trials. To generate TRN and TST sets in CV1 we simply assigned each line to the TST data set, within environment. The same TRN-TST partitions were used to assess the prediction accuracy of each of the models; this yielded 50 correlation estimates for each model, data set, and we report the average correlation (across partitions) and SEs.

RESULTS

Figure 1 shows box-plots of adjusted yield per data set and environmental condition. As expected, average yield increased with the number of irrigation events and, other factors being equal, late planting (H) produced lower yields than normal planting (N). In all cases, the empirical distribution of grain yield within data set and environment was reasonably symmetric.

Table 2 gives the SDs of grain yield for each environment-cycle combination and the (empirical) phenotypic correlations of adjusted grain yield across environments, within cycle. The average SD of grain yield was rather stable across environments, ranging from 0.41 to 0.65. In the first cycle (W1), correlations across environments were moderately positive, ranging from 0.22 to 0.53 and, as one would expect, environments with similar irrigation levels (e.g., 0i and 2i) exhibited greater correlations than environments with very different numbers of irrigations (e.g., 0i vs. 5i). In the second evaluation cycle (W2), three environments received five irrigations (5i) and one received none (0i). The correlations among environments with five irrigations were also moderately positive, ranging from 0.33 to 0.41. However, the correlation between drought environments (0i) and environments having five irrigations was almost zero (−0.05). Finally, in the third evaluation cycle (W3), the two environments with five irrigations and normal planting dates (5iBN and 5iFN) were positively correlated (0.55); however, environments with different irrigation levels or different

Table 6 Estimated prediction accuracy: correlation between predicted and adjusted grain yield, averaged over 50 TRN-TST partitions, cycle 2010–2011 (W1), CV1

| Model/Environmentsa | Correlation | Change%b | Numberc |
|---------------------|-------------|----------|---------|
| Single environment  |             |          |         |
| 0iBN                | 0.530(0.039) | −0.3%; 1.1% | 21; 33  |
| 2iBN                | 0.629(0.038) | −1.6%; 4.3% | 12; 49  |
| 5iBNZ               | 0.472(0.054) | −1%; 24.8% | 8; 49   |
| 5iFN                | 0.486(0.050) | −0.6%; 8%  | 18; 48  |
| Pairs of environments Interaction Between-Env Across-Env | Model | Model | |
| 0iBN                | Cor = 0.53 | 0.529(0.038) | 0.523(0.042) | −0.3%; 1.1% | 21; 33  |
| 2iBN                | Cor = 0.25 | 0.527(0.041) | 0.467(0.045) | −0.6%; 12.8% | 19; 50  |
| 5iBNZ               | Cor = 0.26 | 0.468(0.053) | 0.375(0.052) | −1%; 24.8% | 8; 49   |
| 0iBN                | Cor = 0.34 | 0.633(0.039) | 0.576(0.045) | −0.8%; 10%  | 37; 50  |
| 5iBNZ               | Cor = 0.33 | 0.625(0.041) | 0.555(0.044) | −0.6%; 12.5% | 18; 50  |
| 2iBN                | Cor = 0.22 | 0.466(0.053) | 0.406(0.056) | −1.3%; 14.8% | 15; 50  |
| 5iBNZ               | Cor = 0.22 | 0.483(0.051) | 0.448(0.053) | −0.6%; 8%  | 18; 48  |
| All environments    |             |          |         |
| 0iBN                | Cor = 0.53 | 0.530(0.041) | 0.483(0.048) | 0%; 9.7%  | 24; 49  |
| 2iBN                | Cor = 0.25 | 0.625(0.042) | 0.558(0.046) | −0.5%; 12.1% | 19; 50  |
| 5iBNZ               | Cor = 0.26 | 0.462(0.050) | 0.366(0.051) | −2.2%; 26.3% | 13; 50  |
| 5iFN                | Cor = 0.26 | 0.470(0.049) | 0.394(0.056) | −3.3%; 19.2% | 9; 50   |

TRN-TST, training-testing.
a Environments are described by a sequence of codes: 0i, 2i, and 5i denote the number of irrigation cycles; B/F denotes whether the planting system was “bed” (B) or “flat” (F); N/H denotes whether planting date was normal (N) or late (H, simulating heat); Z indicates no tillage.
b Change in prediction accuracy of the M×E model relative to the prediction accuracy of the single-environment model before semicolon and relative to the prediction accuracy of the across-environment model (after semicolon).
c Number of partitions (of 50) for which the M×E model gave greater accuracy than the single-environment model (before semicolon) and the across-environment model (after semicolon).
planting dates (N/H) showed very low, and even negative, correlations. Interestingly, environments 0iFN and 5iBH, which differ across all factors, showed a moderate sample correlation (0.30).

**Estimates of variance components**

Table 3, Table 4, and Table 5 provide estimates of variance components per model and environment for cycles W1, W2, and W3, respectively. The estimates reported in these tables correspond to the full-data analyses.

**Stratified analysis:** The proportion of variance explained by the regression on markers ($R^2$ computed based on estimates of variance components) estimated from the stratified (single-environment) analysis ranged from moderate (~0.4) to high (~0.7); in general, models fitted data better in W3 (Table 5) than in W1 or W2.

**Across-environment model:** The estimated residual variance of the across-environment model was typically larger (and consequently the $R^2$ was lower) than that of the interaction model indicating that a sizable proportion of the genomic variance went to the residual of the across-environment model.

**MxE model:** In the interaction models, the total genomic variance can be partitioned into a main effect and an interaction component. This partition showed that the relative importance of the main effect was greater when the environments analyzed jointly were positively correlated. On the other hand, as one would expect, when the environments analyzed jointly had low correlations, the estimated interaction variance was greater. For instance, in W1, the analysis of pairs of environments exhibiting sample phenotypic correlations smaller than 0.3 (0iBN + 5iBNZ, 0iBN + 5iFN, and 5iBNZ + 5iFN) yielded estimates of variance components in the MxE model where the main effect explained less than 50% of the total genomic variance, computed as the sum of the main effect plus interaction variance estimates (see Table 3). On the other hand, the pairs of environments showing correlations larger than 0.3 (2iBN + 5iBNZ and 2iBN + 5iFN) gave estimates of variance components where the main effect explained between 50 and 70% of the genomic variance. Finally, in W1, the pair of environments with the largest sample phenotypic correlation (0iFN + 5iBN) had estimates of variance components such that the main effect explained about 80% of the total genomic variance.

Similar patterns were observed in W2 and W3. Indeed, in W2, the main effects of markers explained more than 60% of the genomic variance for pairs of environments having sample phenotypic correlations greater than 0.33 (Table 4); on the other hand, in the two environments showing a low correlation (0iFN + 5iBN), the main effect explained only about 10% of the genomic variance. In W3 data set, pairs of environments with sample phenotypic correlations smaller than 0.1 had an estimated proportion of genomic variance explained by main effects that was smaller than 0.2. At the other extreme, for the pair of environments showing the greatest correlation (5iBNZ + 5iFN), the proportion of variance explained by main effects was close to 0.8 (Table 5). Finally, as expected, in the joint analysis of all environments, the variance of the main effect was largest in W1 and W2 (0.316 and 0.436, respectively), where several pairs of
environments had sample phenotypic correlations that were moderately high, and considerably smaller in W3 (0.113), where many pairs of environments had phenotypic correlations that were negative or close to zero.

**Assessment of prediction accuracy**

The average correlation and the estimated SD (both computed using 50 TRN-TST partitions, each with 70% of records in the TRN data set and 30% in TST data set) obtained in CV1 are reported in Table 6, Table 7, and Table 8 and those obtained in CV2 are reported in Table 9, Table 10, and Table 11. A summary of these results is given in Figure 2. As one would expect, the levels of prediction accuracy (correlation) were slightly greater in CV2 than in CV1. In CV1, the stratified analysis and the interaction model performed similarly (average correlation of 0.48 and 0.47 for the stratified analysis and the interaction model), and the across-environment analysis was the worst one (the average correlation in CV1 was 0.33, that is about 30% lower correlation than the stratification or the interaction model). On the other hand, in CV2, the interaction model gave the greatest levels of prediction accuracy (average correlation 0.53), this method was followed by the stratified analysis (average correlation of 0.48, that is, about 10% less, in the scale of correlation, than the interaction model), and the worst performing method was the across-environment analysis (this method had an average correlation in CV2 of 0.38, that is about 27% less than the interaction model).

**Stratified analysis:**

The within-environment analysis yielded prediction correlations ranging from moderately low (0.307 for environment 5iFN in W3) to moderately high (0.630 for environment 5iBH in W3).

**Across-environment analysis:**

Overall, this method was the worst performing one. In CV1 the across-environment analysis performed worse than the stratified analysis and the interaction model; this in every environment and dataset. In CV2, the joint analysis of data from different environments ignoring G×E performed worse than the

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**Table 8 Estimated prediction accuracy (correlation between predicted and adjusted grain yield, averaged over 50 TRN-TST partitions): cycle 2012–2013 (W3), CV1**

| Models/Environments* | Correlation | Change%b | Numberc |
|-----------------------|-------------|----------|----------|
| **Single environment** |             |          |          |
| 0iFN                  | 0.561(0.035) |          |          |
| 2iBN                  | 0.445(0.051) |          |          |
| 5iBH                  | 0.628(0.037) |          |          |
| 5iBN                  | 0.360(0.046) |          |          |
| 5iFN                  | 0.312(0.055) |          |          |
| **Pairs of environments** |           |          |          |
| 0iFN 2iBN             | 0.559(0.036) | 0.411(0.049) | -0.3%; 36.1% | 18; 50 |
| 0iFN 5iBH             | 0.563(0.036) | 0.466(0.042) | 0.2%; 20.7% | 34; 50 |
| 0iFN 5iBN             | 0.559(0.036) | 0.356(0.048) | -0.5%; 57.1% | 13; 50 |
| 0iFN 5iFN             | 0.360(0.046) | 0.154(0.051) | -0.1%; 134.2% | 27; 50 |
| 0iFN 5iFN             | 0.357(0.046) | 0.156(0.048) | -0.7%; 129.5% | 20; 50 |
| 2iBN 5iBH             | 0.441(0.052) | 0.236(0.049) | -0.7%; 87.2% | 11; 50 |
| 2iBN 5iBN             | 0.625(0.037) | 0.439(0.052) | 0.4%; 42.3% | 9; 50 |
| 2iBN 5iFN             | 0.444(0.051) | 0.370(0.049) | -0.1%; 20.2% | 27; 49 |
| 2iBN 5iBN             | 0.361(0.046) | 0.300(0.047) | 0.2%; 20.2% | 31; 48 |
| 2iBN 5iFN             | 0.446(0.050) | 0.345(0.052) | 0.3%; 29.4% | 31; 50 |
| 2iBN 5iFN             | 0.313(0.054) | 0.180(0.056) | 0.1%; 73.7% | 24; 50 |
| 5iBH 5iBN             | 0.627(0.038) | 0.451(0.051) | -0.2%; 38.9% | 14; 50 |
| 5iBH 5iBN             | 0.358(0.046) | 0.130(0.054) | -0.6%; 174.4% | 20; 50 |
| 5iBH 5iBN             | 0.625(0.038) | 0.485(0.046) | -0.4%; 28.8% | 10; 50 |
| 5iBN 5iBN             | 0.305(0.053) | 0.125(0.060) | -2.2%; 144.1% | 7; 50 |
| 5iBN 5iBN             | 0.352(0.046) | 0.316(0.052) | -2.2%; 11.5% | 15; 46 |
| 5iFN 5iFN             | 0.309(0.053) | 0.286(0.054) | -1.2%; 79.2% | 19; 42 |

**TRN-TST:** training-testing.

*Environments are described by a sequence of codes: 0i, 2i, and 5i denote the number of irrigation cycles; B/F denotes whether the planting system was “bed” (B) or “flat” (F); N/H denotes whether planting date was normal (N) or late (H, simulating heat); Z indicates no tillage.

*Change in prediction accuracy of the M×E model relative to the prediction accuracy of the single-environment (before semicolon) and relative to the prediction accuracy of the across-environment model (after semicolon).

*Number of partitions (out of 50) for which the M×E model gave greater accuracy than the single-environment (before semicolon) and the across-environment model (after semicolon).
stratified analysis when the pairs of environments analyzed together had a correlation lower than 0.3; however, the across-environment model tended to outperform the stratified analysis whenever the correlation between environments was larger than 0.4. On the other hand, the interaction model: (i) is easy to implement using existing software for GS; (ii) leads to a decomposition of marker effects into QTL models by Moreau et al. (2004), Van Eeuwijk et al. (2005), Boer et al. (2007), and Malosetti et al. (2004, 2008), to whole-genome regression models where phenotypes were regressed on large numbers of genome-wide markers.

**DISCUSSION**

Several studies have documented the benefits of using multienvironment models, relative to single-environment analysis (Burgueño et al. 2012; Dawson et al. 2013; Jarquin et al. 2014). Multienvironment analysis can model G×E interactions using covariance functions (Burgueño et al. 2012), markers and environmental covariates (Jarquin et al. 2014; Heslot et al. 2014), or by modeling M×E interactions. In this article, we adapted this approach, previously used in QTL models by Moreau et al. (2004), Van Eeuwijk et al. (2005), Boer et al. (2007), and Malosetti et al. (2004, 2008), to whole-genome regression models where phenotypes were regressed on large numbers of genome-wide markers.

Relative to the standard multienvironment models with structured or unstructured covariances such as those used by Burgueño et al. (2012), the M×E model has advantages and disadvantages. On one hand, the interaction model: (i) is easy to implement using existing software for GS; (ii) leads to a decomposition of marker effects into

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### Table 9 Estimated prediction accuracy: correlation between predicted and adjusted grain yield, averaged over 50 TRN-TST partitions, cycle 2010–2011(W1), CV2

| Model/Environments | Correlation (SE) | Change% | Number |
|--------------------|------------------|---------|--------|
| Single environment |                  |         |        |
| 0iBN               | 0.529(0.044)     | –       | –      |
| 2iBN               | 0.622(0.045)     | –       | –      |
| 5iBN               | 0.452(0.051)     | –       | –      |
| 5iFN               | 0.493(0.046)     | –       | –      |

| Pairs of environments | Interaction Model | Across-Env Model | Change% | Number |
|-----------------------|------------------|-----------------|---------|--------|
| 0iBN                  | 0.599(0.036)     | 0.590(0.040)    | 13.3%; 1.5%; 50; 36 |
| 2iBN                  | 0.687(0.034)     | 0.664(0.037)    | 10.5%; 3.5%; 50; 47 |
| 0iBN                  | 0.547(0.040)     | 0.476(0.049)    | 3.5%; 14.9%; 49; 50 |
| 5iBNZ                 | 0.467(0.050)     | 0.380(0.051)    | 3.4%; 23.1%; 48; 49 |
| 0iBN                  | 0.544(0.038)     | 0.486(0.042)    | 3.0%; 12.0%; 46; 48 |
| 5iBNZ                 | 0.452(0.048)     | 0.452(0.048)    | 1.7%; 10.8%; 45; 48 |
| 0iBN                  | 0.661(0.037)     | 0.587(0.042)    | 6.3%; 12.6%; 50; 50 |
| 5iBNZ                 | 0.450(0.044)     | 0.445(0.040)    | 9.8%; 11.4%; 49; 46 |
| 2iBN                  | 0.648(0.043)     | 0.556(0.057)    | 4.2%; 16.5%; 44; 50 |
| 5iBNZ                 | 0.507(0.047)     | 0.456(0.054)    | 2.8%; 11.3%; 47; 49 |
| 5iFN                  | 0.476(0.052)     | 0.406(0.057)    | 5.4%; 17.2%; 33; 50 |
| 5iFN                  | 0.491(0.047)     | 0.450(0.062)    | –0.4%; 9.2%; 35; 44 |

| All environments      |                  |         |        |
|-----------------------|------------------|---------|--------|
| 0iBN                  | 0.591(0.040)     | 0.531(0.047) | 11.8%; 11.3%; 50; 50 |
| 2iBN                  | 0.697(0.033)     | 0.645(0.034) | 12.1%; 8.2%; 50; 50 |
| 5iBNZ                 | 0.505(0.047)     | 0.399(0.050) | 11.9%; 26.8%; 50; 50 |
| 5iFN                  | 0.516(0.051)     | 0.429(0.059) | 4.7%; 20.4%; 41; 50 |

TRN-TST, training-testing.

a Environments are described by a sequence of codes: 0, 2, and 5i denote the number of irrigation cycles; B/F denotes whether the planting system was “bed” (B) or “flat” (F); N/H denotes whether planting date was normal (N) or late (H, simulating heat); Z indicates no tillage.

b Change in prediction accuracy of the M×E model relative to the prediction accuracy of the single-environment (before semicolon) and relative to the prediction accuracy of the across-environment model (after semicolon).

c Number of partitions (of 50) for which the M×E model gave higher accuracy than the single-environment (before semicolon) and the across-environment model (after semicolon).
components that are stable across environments (main effects) and environment-specific deviations (interactions) that can shed light on which genomic regions are most responsible for GxE; and (iii) can be implemented with any of the priors commonly used in GS, including not only shrinkage methods such as the GBLUP, but also variable selection methods. On the other hand, the MxE model imposes restrictions on co-variance patterns: the covariance is represented by the variance of the main effects and, along the lines of full irrigation, drought, and heat than based on whether they include beds or flat planting systems, and zero or conventional tillage.

### Variance components

The MxE model fitted the data much better than the across-environment model that ignored GxE. Furthermore, the estimates of variance components from the MxE model indicated that the proportion of genomic variance explained by the main effect of markers is directly related to the (sample empirical) phenotypic correlation between environments. Analytically, under the assumptions of the MxE model described and used in this article, if $y_{i1} = \mu_1 + u_{i1} + e_{i1}$ and $y_{i2} = \mu_2 + u_{i2} + e_{i2}$ are the equations for the phenotype of the $i$th line in environments 1 and 2, respectively, then the phenotypic correlation can be expressed as a function of variance components, indeed $Cor(y_{i1}, y_{i2}) = \frac{\text{Cov}(y_{i1}, y_{i2})}{\sqrt{\text{Var}(y_{i1})\text{Var}(y_{i2})}} = \frac{\sigma_y^2}{\sqrt{\sigma_u^2 + \sigma_e^2 + \sigma_i^2}}$. Figure 3 displays the estimated phenotypic correlations derived using estimates of variance components obtained from analyses based on pairs of environments (see Table 3, Table 4, and Table 5) vs. the observed sample phenotypic correlations. Overall, the estimated phenotypic correlation based on variance components was linearly related to the sample phenotypic correlation for pairs of environments having positive sample phenotypic correlations. However, as the sample phenotypic correlation approached zero or became negative, the relationship flattened out. This happens because, in the interaction model, the covariance is represented by the variance of the main effects and, therefore, it is bound to be non-negative.
Prediction accuracy

The prediction analysis conducted in this study yielded levels of accuracy (correlation between phenotypes and predicted genomic values) that are consistent with previous reports for grain yield prediction accuracy using single- and multi-environment models (Burgueño et al. 2012). Overall, the interaction model was either the best performing method (CV2) or performed close to the best performing method (in CV1 the stratified analysis and the interaction model performed similarly). These results are consistent with those of previous studies (e.g., Burgueño et al. 2012; Jarquin et al. 2014) that have used similar validation designs (CV1 and CV2) and have reported similar predictive performance of the stratified and multivariate analysis in CV1, and clear superiority of the multivariate approach in CV2. Additionally, we also considered an across-environment analysis that ignores G×E. In our study this approach was clearly the worst-performing one; this finding highlights the importance of considering G×E when analyzing multi-environment data.

The gains in prediction accuracy obtained in CV2 with the M×E model were directly related to the correlations between environments. Considering environments that had positive phenotypic correlations among them, the use of the M×E model yielded in CV2 gains, relative to the stratified analysis, that were either moderate (on the order of 5%) or very substantial (on the order of 29%). In CV2 the only cases where the stratified analysis was better than the interaction model are those based on the joint analysis of pairs of environments that had close to null or negative correlations (e.g., 5iBH in W3). This happened because, as discussed previously, the interaction model forces the covariance between environments to be non-negative.

In prediction problems such as that of CV2, the superiority of the M×E relative to the stratified analysis can be attributed to the fact that the M×E model allows borrowing of information within line across environments, that is: when deriving predictions for a given line, the M×E model benefits from records from the same line collected in correlated environments (this borrowing of information also happens in the across-environment GBLUP; however, in the across-environment GBLUP borrowing of information within line across environments is achieved at the expense of forcing the effects to be constant across environments). This feature of the M×E model can be exploited.
in prediction problems such as CV2; however, such borrowing of information within line is not possible in CV1 and, consequently, the MxE model performs similarly to the stratified analysis for prediction of performance of lines that have no phenotypic records.

How many environments?
The interaction model can be applied to all available environments or to other sets (e.g., pairs) of environments. For data sets such as W1, where all environments showed positive correlations of similar magnitude, the joint analysis of all environments was clearly superior to analyses based on pairs of environments. However, in data sets exhibiting complex covariance patterns (such as W3), joint analysis of all environments using an interaction model imposes inadequate restrictions on co-variance patterns and, consequently, bivariate analysis seems more appropriate.

Extensions
In our study, because of the limitations of the software used, we implemented the MxE model in which the error variance was assumed to be homogeneous across environments. In principle, the model can be easily extended to accommodate environment-specific variances.

In this study, we presented and applied the interaction model using Gaussian priors. We did this because the GBS marker data contain a large proportion of missing values. However, with high-density panels of high-quality markers (e.g., single-nucleotide polymorphisms) it would make perfect sense to use other priors. For instance, it could be used with priors that induce differential shrinkage of estimates or variable selection (de los Campos et al. 2013); such treatment would potentially aid in identifying sets of markers with effects that are stable across environments and others that are responsible for GxE.

The MxE model presented in this article is an easy-to-implement and easy-to-interpret approach for modeling GxE in genomic models. The model allows decomposing marker effects and genomic variance into components that are stable across environments (main effects) and components that are environment-specific (interaction terms). The model can be implemented easily using existing software for GS. Predictions from the interaction model had either similar (CV1) or greater (CV2) accuracy than the single-environment analysis and were always more accurate than those derived from an across-environment analysis that ignored GxE; therefore, the proposed model should be useful for selection based on either stability (main effects only) or for target environments (based on total genomic value). The interaction model is not free of limitations; in particular, it is important to note that the genetic covariance between any pair of environments is represented by the variance of the main effect; therefore, it is restricted to being positive and the same for all pairs of environments analyzed jointly. Therefore, the model should be more effective when applied to subsets of environments that have positive and similar correlations.

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