Persistency of Prediction Accuracy and Genetic Gain in Synthetic Populations Under Recurrent Genomic Selection

Dominik Müller,1 Pascal Schopp,1 and Albrecht E. Melchinger2
Institute of Plant Breeding, Seed Sciences and Population Genetics, University of Hohenheim, 70599 Stuttgart, Germany

ABSTRACT Recurrent selection (RS) has been used in plant breeding to successively improve synthetic and other multiparental populations. Synthetics are generated from a limited number of parents (Np), but little is known about how Np affects genomic selection (GS) in RS, especially the persistency of prediction accuracy (rg) and genetic gain. Synthetics were simulated by intermating Np = 2-32 parent lines from an ancestral population with short- or long-range linkage disequilibrium (LDg) and subjected to multiple cycles of GS. We determined rg and genetic gain across 30 cycles for different training set (TS) sizes, marker densities, and generations of recombination before model training. Contributions to rg and genetic gain from pedigree relationships, as well as from cosegregation and LDg between QTL and markers, were analyzed via four scenarios differing in (i) the relatedness between TS and selection candidates and (ii) whether selection was based on markers or pedigree records. Persistency of rg was high for small Np, where predominantly cosegregation contributed to rg, but also for large Np, where LDg replaced cosegregation as the dominant information source. Together with increasing genetic variance, this compensation resulted in relatively constant long- and short-term genetic gain for increasing Np > 4, given long-range LDg in the ancestral population. Although our scenarios suggest that information from pedigree relationships contributed to rg for only very few generations in GS, we expect a longer contribution than in pedigree BLUP, because capturing Mendelian sampling by markers reduces selective pressure on pedigree relationships. Larger TS size (NTS) and higher marker density improved persistency of rg and hence genetic gain, but additional recombinations could not increase genetic gain.

KEYWORDS
- genomic selection
- recurrent selection
- synthetic populations
- prediction accuracy
- genetic gain
- GenPred
- Shared Data Resources
- Genomic Selection

RS is an integral tool in plant breeding that targets the systematic improvement of quantitative traits in broad-based populations by increasing the frequency of favorable alleles, while maintaining genetic variability (Hallauer and Carena 2012). Source materials in allogamous crops include open-pollinated and synthetic populations (synthetics, Hallauer 1992). Synthetics are created by intermating a limited number of parental components and cross-pollinating the progeny for one or several generations (Falconer and Mackay 1996). A prominent example is the Iowa Stiff Stalk Synthetic (BSSS), which was developed from 16 inbred lines in the 1930s and has since been subjected to two long-term RS programs (Hallauer 2008), which have contributed a large proportion of today’s commercial maize germplasm (Mikel and Dudley 2006).

GS is a novel statistical method (Meuwissen et al. 2001) with the capability to accelerate future genetic progress in plant breeding (Heffner et al. 2010). Several studies indicate a potential superiority of GS over phenotypic selection (Bernardo 2009; Wong and Bernardo 2009; Jannink 2010; Yabe et al. 2013), marker-assisted selection (Bernardo and Yu 2007; Wong and Bernardo 2009; Heffner et al. 2010, Yabe et al. 2013), as well as pedigree-based selection (Muir 2007; Wolc et al. 2011a, 2016; Bastiaansen et al. 2012; Van Grevenhof et al. 2012). Although the usefulness of GS across two selection cycles has empirically been demonstrated in biparental maize families...
GS has further been proposed as a particularly suitable tool for RS in synthetics (Windhausen et al. 2012; Gorjanc et al. 2016). In this context, an established prediction equation could be used repeatedly for multiple cycles of selection without retraining. Combined with the use of off-season nurseries, this promises to increase genetic gain per unit time and to reduce costs for phenotyping (Bernardo and Yu 2007). The success of this strategy largely depends on persistency of the $r_{g\delta}$ of estimated breeding values (EBV) across selection cycles to ensure satisfactory genetic gain when selection candidates are separated by one or more cycles from the model training generation. Although formulas for forecasting $r_{g\delta}$ in a single cycle were derived (Daetwyler et al. 2008; Hayes et al. 2009; Goddard 2009; Goddard et al. 2011), no closed analytical solutions are available for calculating $r_{g\delta}$, the additive genetic variance ($\sigma_g^2$) and the cumulative genetic gain ($\sum \Delta G$) across several selection cycles. This is because changes in the LD pattern, allele frequencies, and loss of polymorphisms are unpredictable (Jannink 2010).

While empirical results on persistency of $r_{g\delta}$ in actual plant breeding programs are scarce to date, several simulation studies across multiple generations investigated $r_{g\delta}$ of GS, assuming random mating of the whole population between generations (Meuwissen et al. 2001; Habier et al. 2007; Nielsen et al. 2009; Solberg et al. 2009). Others assumed selection and were therefore able to evaluate potential genetic gain using GS (Muir 2007; Sonesson and Meuwissen 2009; Jannink 2010; Bastiaansen et al. 2012; Yabe et al. 2013, 2016; Liu et al. 2015). However, these studies generally considered fairly large effective population sizes $N_e \approx 100$, which are unrealistic for synthetics in plant breeding. In synthetics, the number of parents is usually relatively small and parents are often related, leading to small $N_e$ of the population. It is yet unclear how such a small $N_e$ influences the persistency of $r_{g\delta}$ in genomic RS.

Initially, LD between QTL and molecular markers (commonly SNPs) of high density maps was considered as the only source of information exploited in GS (Meuwissen et al. 2001). In synthetics, LD between QTL and SNPs is attributable to (i) LD$_{g\delta}$ in the population from which the parents were taken, and (ii) sample LD, randomly generated by using a restricted number of parents $N_p$. (Schopp et al. 2017). Sample LD is conserved from parents to progeny by cosegregating loci, and has therefore been termed cosegregation. However, it was also demonstrated that SNPs contribute to $r_{g\delta}$ by capturing pedigree relationships between individuals (Habier et al. 2007). Research in a companion paper (Schopp et al. 2017) showed that the choice of $N_p$ in synthetics crucially affects the relative importance of LD$_{g\delta}$ and cosegregation as well as the contribution of pedigree relationships in a single cycle of GS in synthetics. However, no study systematically investigated the importance of these information sources for the persistency of $r_{g\delta}$ and $\sum \Delta G$ in recurrent GS.

Besides the choice of $N_p$, an important question is how often the source material should be recombined before starting RS. Additional recombination might release genetic variability useful for long-term genetic gain (Schnable et al. 1996). For instance, Bernardo (2009) recommended the use of F$_2$ instead of F$_1$ plants in the production of maize doubled haploids. However, additional recombination might also adversely affect the three information sources in GS, and so far studies have not addressed whether this can outweigh the potential increase in long-term genetic gain.

In the present study, we applied fully stochastic forward-in-time simulations and generated two ancestral populations differing substantially in LD$_{g\delta}$. From these, we sampled different numbers of parents $N_p$ to create synthetics that were subjected to multiple cycles of recurrent GS, either directly or after additional generations of recombination. Our objectives were to (i) analyze $r_{g\delta}$ and $\sum \Delta G$ in recurrent GS, depending on the number of parents $N_p$, LD$_{g\delta}$, and the number of recombination generations $N_R$, and (ii) determine the importance of the three information sources, considering also NS and SNP density. Finally, we discuss implications for practical decisions in breeding programs employing recurrent GS.

**METHODS**

**Genome properties and simulation of ancestral populations**

Properties of the genome, construction of the genetic map, and simulation of ancestral populations are detailed in Schopp et al. (2017). In brief, we selected maize (Zea mays L.) as a model species using genetic map positions for 37,286 SNPs distributed over 10 chromosomes with 1913 cM in total. Using the software QMSim (Sargolzaei and Schenkel 2009), we simulated two ancestral populations with either short-range LD$_{g\delta}$ (SR) or extensive long-range LD$_{g\delta}$ (LR). First, we generated an initial population of 1500 diploid individuals by sampling alleles at each (biallelic) locus independently from a Bernoulli distribution with probability 0.5. Second, 5000 loci were randomly sampled from all SNPs and henceforth interpreted as QTL; all remaining loci were considered as SNP markers. Third, these individuals were randomly mated for 3000 generations with a constant population size of 1500 and a mutation rate of $2 \times 10^{-5}$ until mutation-drift-equilibrium was reached. Fourth, a strong population bottleneck was imposed by reducing the population size to 30 arbitrarily selected individuals, followed by 15 additional generations of random mating to generate extensive long-range LD$_{g\delta}$. Lastly, the population was expanded to 10,000 individuals and randomly mated three times more to establish ancestral population LR. Ancestral population SR was derived from LR by continuing random mating for 100 generations with constant population size of 10,000 to break down long-range LD$_{g\delta}$. Due to this large population size, genetic drift had only a negligible influence and hence allele frequencies were nearly identical in both ancestral populations. The heterozygous ancestral populations (LR and SR) were considered as unrelated and were used as reference bases for the pedigree of all subsequently derived individuals.

**Simulation of synthetic populations**

The RS breeding scheme applied is shown in Figure 1 and factors analyzed are listed in Table 1. The simulation of the synthetics varied, depending on whether the parents of the TS and the recurrent selection candidates (RSC) were identical ($P_{TS} = P_{RSC}$) or disjoint ($P_{TS} \cap P_{RSC} = \emptyset$). For $P_{TS} = P_{RSC}$, a single synthetic was simulated from which both the TS and the RSC were sampled, whereas for $P_{TS} \cap P_{RSC} = \emptyset$ TS and RSC were taken from two synthetics having no parents in common. In both cases, $N_p \in \{2, 3, 4, 6, 8, 12, 16, 32\}$ parental gametes were randomly drawn from the same ancestral population and chromosomes were doubled in silico to generate fully homozygous parent lines. These were inbred to obtain all possible $[N_p(N_p-1)]/2$ single crosses, denoted as generation Syn$_{N_p}$. Subsequently, single crosses were randomly mated $N_R$ times (allowing for selfings) to obtain generation Syn$_{N_R}$, from which the TS (Syn$_{N_R}^{TS}$) and RSC (Syn$_{N_R}^{RSC}$) were later drawn. Here, $N_R \in \{1, 2, 3, 4, 5\}$ counts the number of recombination generations conducted prior to initiating RS. For the special case of $N_p = 2$, the Syn$_0$ corresponded to a F$_1$ cross and Syn$_1$ to a F$_2$ family.

**Genetic model**

We assumed a quantitative trait based on 1000 biallelic QTL with purely additive gene action and absence of QTL × year interactions. For each simulation replicate, QTL were randomly sampled from the 37,286...
SNPs present in the ancestral population. Following Meuwissen et al. (2001), absolute values of QTL effects were drawn from a gamma distribution with scale and shape parameter of 0.4 and 1.66, respectively. Signs of QTL effects were sampled from a Bernoulli distribution with probability 0.5. Although we assumed biallelic QTL, the alleles of neighboring QTL are strongly correlated due to LD\(_A\) and linkage, effectively leading to haploblocks that could be considered as higher-level multi-allelic QTL. The true breeding value (TBV) \(g_i\) for any individual \(i\) (either from the synthetics or from the ancestral populations) was computed as \(g_i = \sum_{j=1}^{m} W_{ij} a_j\), where \(W_{ij}\) counts the number of minor alleles at the \(j\)-th QTL centered by the respective ancestral allele frequency in LR, and \(a_j\) is the associated QTL effect. Phenotypes \(y_i\) were simulated as \(y_i = g_i + e_i\), where \(e_i \sim N(0, \sigma^2_e)\) is an environmental noise variable. The error variance \(\sigma^2_e\) was assumed to be constant throughout all simulations and was determined as follows: for all individuals in the ancestral population LR, TBVs were calculated according to the above procedure under replicated sampling of 1000 QTL together with their associated effects. The variance of the noise variable \(\sigma^2_e\) was then set equal to the mean additive genetic variance \(\sigma^2_A\). As the allele frequencies in both ancestral populations were virtually identical, \(\sigma^2_A\) was also the mean additive genetic variance in ancestral population SR. This approach implies that the heritability in ancestral populations LR and SR was, on average, 0.5. Heritability was lower in the synthetics due to the finite sample of parents and, on average, \(h^2 \rightarrow 0.5\) for \(N_p \rightarrow 20,000\).

**Information source scenarios**

We employed four distinct scenarios to evaluate the contributions of the three information sources used in Genomic Best Linear Unbiased Prediction (GBLUP) for estimating actual relationships at causal loci by SNPs (cf. Habier et al. 2013). These scenarios can be distinguished by (i) the relatedness of the TS and RSC and (ii) the type of data employed for calculating the relationship matrix used as a kernel in GBLUP (Supplemental Material, Table S1).

Our standard scenario was \(Re - LD_A - SNP\), where the TS and RSC were related (Re) as their parents were identical (\(PT_S = P_{RSC}\)). The kernel in GBLUP was calculated based on SNPs (excluding QTL) and thus contained genomic relationships. As a consequence, this scenario harnesses all three sources of information, namely: (i) pedigree relationships captured by SNPs, (ii) cosegregation between QTL and SNPs by virtue of the parents being identical, and (iii) \(LD_A\) between QTL and SNPs due to the presence of \(LD_A\) in the ancestral population, which was carried over to the synthetics. \(Re - LD_A - SNP\) is a realistic scenario and is perhaps the most frequent scenario encountered in applications of GS.

Scenario \(Re - LE_A - SNP\) was artificial and was derived from \(Re - LD_A - SNP\). Here, for each of the 10 chromosomes, the multilocus genotypes of QTL and SNPs were regarded as separate units and were reshuffled among the \(N_p\) parents prior to intermating. This procedure broke up historical associations between QTL and SNPs due to \(LD_A\), while conserving the LD structure among QTL and among SNPs as well as their allele frequencies. Hence, information from \(LD_A\) cannot contribute to \(r_{qg}\) and any LD between QTL and SNPs is exclusively due to sampling a limited number of parental gametes from the ancestral population, i.e., sample LD.

Scenario \(Re - LD_A - Ped\) was identical to \(Re - LD_A - SNP\) except that the kernel of GBLUP was the numerator relationship matrix calculated from pedigree records of all individuals (pedigree BLUP). This scenario provided a reference for \(r_{qg}\) and its dynamics across cycles that can be obtained exclusively from known pedigree relationships between TS and RSC.

In scenario \(Un - LD_A - SNP\), the TS and RSC were unrelated (Un), because their parents were distinct (\(PT_S \cap P_{RSC} = \phi\)). Thus, the influence of pedigree relationships captured by SNPs and cosegregation between QTL and SNPs is eliminated, and the only remaining connection between the TS and RSC is the LD shared due to their common ancestral population, i.e., \(LD_A\).

**Genomic prediction model**

We used GBLUP to predict breeding values \(g_i\) according to the model equation

\[
y_i = \mu + g_i + \epsilon_i,
\]

where \(y_i\) and \(g_i\) are the phenotypic and breeding values, respectively, of the \(i\)-th individual, \(\mu\) is the overall population mean, and \(\epsilon_i\) the
associated model residual. Standard assumptions about the distribution of the random effects were \((g_i) \sim MVN(0, \sigma_g^2K), (\varepsilon_i) \sim MVN(0, \sigma_e^2I)\), and stochastic independence of \((g_i)\) and \((\varepsilon_i)\).

Variance component estimates for \(\sigma_g^2\) and \(\sigma_e^2\), as well as predicted breeding values were calculated using the R-package rRBLUP (Endelman 2011). The matrix \(\sigma_g^2K=(\sigma_g^2k_{ij})\) describes the variance-covariance structure of the breeding values of all individuals (TS and RSC) and was computed based on different types of data, depending on the information scenario. For Re – LD\(_A\) – SNP, Re – LE\(_A\) – SNP, and Un – LD\(_A\) – SNP, SNP-based genomic relationship coefficients \(k_{ij}\) between individuals \(i\) and \(j\) were computed following VanRaden (2008) as

\[
k_{ij} = \frac{\sum_k(x_{ik} - 2p_k)(x_{jk} - 2p_k)}{\sum_k 2p_k(1 - p_k)},
\]

where \(x_{ik}, x_{jk} \in \{0, 1, 2\}\) are the genotypic SNP scores and \(p_k\) is the frequency at the \(k\)-th SNP marker in the ancestral population. In scenario Re – LD\(_A\) – Ped, pedigree relationships were computed from the complete pedigree records of all individuals using the R-package pedigree (Coster 2013).

Recurrent genomic selection scheme

The TS was sampled once from synthetic Syn\(_{N_0}\) (Figure 1) and thereafter used to predict breeding values in all of 30 selection cycles. The initial 100 RS candidates were sampled from the remaining individuals of Syn\(_{N_0}\) if \(P_{TS} = P_{RSC}\), or from the second synthetic Syn\(_{N_0}\); \(P_{TS} \cap P_{RSC} = \emptyset\). In each cycle, the top \(N_p = 10\) individuals were selected (before flowering) either based on (i) EBV calculated by GBLUP or pedigree BLUP (scenario Re – LD\(_A\) – Ped), (ii) TBV, corresponding to phenotypic selection with \(h^2 = 1\), or (iii) “random breeding values” (RBV), being chosen at random. While EBV shows the realistic decay of \(r_{g,\delta}\) (taking into account that \(r_{g,\delta}\) in earlier cycles influences \(r_{g,\delta}\) in later cycles), TBV provides an identical and constant selection accuracy of one, independent of \(r_{g,\delta}\) for all scenarios. RBV shows the decay of \(r_{g,\delta}\) without directional selection, i.e., the decay that is caused by recombination and genetic drift alone. The selected fraction of 10% is realistic for practical applications and has been used in other simulation studies (e.g., Jannink 2010). The selected candidates were subsequently recombined by random mating to create 100 new progeny, serving as RSC in the next selection cycle. The effects of \(N_{TS} \in \{250, 1000\}\) and of SNP density \(\{0.125, 2.5\}\) were examined in independent simulations, with default values of \(N_{TS} = 250\) and \(2.5\) SNPs. For each combination of factors, we conducted 500 independent simulation replicates. Here, one replicate encompasses: (i) sampling of \(N_p\) parents from the ancestral population; (ii) sampling of 1000 QTL together with their QTL effects and an appropriate number of SNPs to reach the desired marker density; (iii) creation of the synthetics assuming different numbers of generations of random mating, and sampling of the TS and the initial RSC; (iv) simulation of phenotypes for TS individuals; and (v) conduction of recurrent GS without retraining for 30 selection cycles. All simulations were performed with the R statistical language (R Core Team 2015) and code is provided in File S2.

Cumulative genetic gain, additive genetic variance, and prediction accuracy

In each selection cycle, the cumulative genetic gain \(\sum \Delta G\) was computed as the average of all 100 TBVs \(g_i\) of the RSC relative to the average in \(C = 0\). The \(\sigma_g^2\) of the RSC was computed as the variance of \(g_i\) values. The \(\sum \Delta G\) was expressed in units of \(\sigma_g^2(anc)\) and \(\sigma_g^2\) in units of \(\sigma_g^2(anc)\). \(r_{g,\delta}\) was calculated as the Pearson correlation coefficient between TBVs \(g_i\) and predicted breeding values \(\hat{g}_i\) of the RSC.

Data availability

The authors state that all data necessary for confirming the conclusions presented in the article are represented fully within the article.

RESULTS

Dynamics of genetic gain, prediction accuracy, and additive genetic variance

An overview of the dynamics of cumulative genetic gain \(\sum \Delta G\) and prediction accuracy \(r_{g,\delta}\) under recurrent GS for the standard scenario Re – LD\(_A\) – SNP is given in Figure 2. Across selection cycles, \(\sum \Delta G\) increased concavely, approaching a plateau. Regardless of the number of parents \(N_p\), \(\sum \Delta G\) was higher in LR compared to SR. For LR, \(\sum \Delta G\) increased together with \(N_p\), whereas for SR, \(\sum \Delta G\) was lowest for \(N_p = 2\), highest for \(N_p = 4\), and intermediate for \(N_p = 16\). In the model training generation (\(C = 0\)), \(r_{g,\delta}\) ranged between 0.7 and 0.8 and was higher for smaller \(N_p\). After the first round of selection, there was a substantial decline in \(r_{g,\delta}\) that was strongest for large \(N_p\), \(r_{g,\delta}\) generally approached an asymptotic value of \(\sim 0.1\) in cycle \(C = 30\). The overall level of \(\sigma_g^2\) (Figure S1) in the RSC was higher for larger \(N_p\) and strongly declined during selection, especially after the first cycle. In \(C = 0\), \(\sigma_g^2\) was nearly identical for LR and SR, and showed a slightly steeper decline in LR.
Cumulative genetic gain

To explore in greater detail $\sum \Delta G$ in $C = 30$ and the information sources primarily exploited, we varied $N_p$ between 2 and 32 (Figure 3). Here, the relationship between $\sum \Delta G$ and $N_p$ in scenario $Re - LD_A - SNP$ was strongly affected by the level of $LD_A$. For LR, $\sum \Delta G$ initially increased between $N_p = 2$ and $N_p = 8$ and then remained nearly constant for larger $N_p$. For SR, $\sum \Delta G$ also increased initially, but then strongly decreased for larger $N_p$. In scenario $Un - LD_A - SNP$ ($P_{TS} \cap P_{RSC} = o$), $\sum \Delta G$ was much lower than in $Re - LD_A - SNP$ and monotonically increased with growing $N_p$. This increase and the overall level of $\sum \Delta G$ was much higher in LR than SR. In scenario $Re - LD_A - Ped$, $\sum \Delta G$ was zero for $N_p = 2$, and strongly increased with $N_p$, plateauing at $8 \leq N_p \leq 12$. For scenario $Re - LD_A - Ped$, virtually no further genetic gain could be realized after $C = 2$ (Figure S2).

Persistence of prediction accuracy

The persistency of $r_{g,g}$ for selection regimes $EBV$, $TBV$, and $RBV$ under LR is shown in Figure 4. For scenarios $Re - LD_A - SNP$ and $Re - LE_A - SNP$, the overall level of $r_{g,g}$ declined with growing $N_p$, whereas it increased for scenario $Un - LD_A - SNP$ (compare Figure S3). In scenario $Re - LD_A - SNP$, the decay of $r_{g,g}$ was strongest in the first selection cycle, especially for large values of $N_p$. In scenario $Re - LD_A - Ped$, $r_{g,g}$ could not be calculated for $N_p = 2$ and $N_p = 1$, as discussed in File S1; for $N_p > 2$, $r_{g,g}$ started at $C = 0$ at intermediate values of $\sim 0.5$ for $N_p = 4$ and $\sim 0.6$ for $N_p = 16$ but declined to zero within a few cycles if the selection was based on either $EBV$ or $TBV$. With selection based on $RBV$, $r_{g,g}$ approached zero only for $C > 10$. Scenarios $Re - LD_A - SNP$ and $Re - LE_A - SNP$ showed identical $r_{g,g}$ for $N_p = 2$. For $N_p > 2$, $r_{g,g}$ decreased faster in $Re - LE_A - SNP$ than in $Re - LD_A - SNP$ and more so with increasing $N_p$. When ancestral long-range $LD_A$ was absent (SR), the differences between $Re - LE_A - SNP$ and $Re - LD_A - SNP$ were generally much smaller, but otherwise trends were similar (results not shown). Scenario $Un - LD_A - SNP$ showed an overall low level of $r_{g,g}$, especially for SR, where it was close to zero. However, the decline of $r_{g,g}$ across cycles was attenuated compared to the other scenarios. When selection was exercised based on $TBV$, the decay of $r_{g,g}$ was similar to selection based on $EBV$, but much stronger compared with selection based on $RBV$.

TS size and SNP density

The influence of $N_{TS}$ and SNP density on $r_{g,g}$ under selection based on $EBV$ is shown in Figure 5. For all scenarios, increasing $N_{TS}$ elevated the level of $r_{g,g}$ across cycles. Specifically, for scenarios assuming $P_{TS} = P_{RSC}$, increasing $N_{TS}$ reduced the drop in $r_{g,g}$ after the first selection cycle, which was not observed for scenario $Un - LD_A - SNP$ ($P_{TS} \cap P_{RSC} = o$). Increasing marker density from 0.125 to 2.5 cm$^{-1}$ notably increased the level of $r_{g,g}$ for all SNP-based scenarios and led to higher persistency of $r_{g,g}$ for SNP-based scenarios with identical parents ($P_{TS} = P_{RSC}$). Scenario $Un - LD_A - SNP$ did not show an increased persistency with higher marker density.

Number of recombinations

In general, increasing the number of recombinations $N_R$ resulted in a decrease of $r_{g,g}$ ($C = 0$, Figure 6), except for scenario $Un - LD_A - SNP$, where $r_{g,g}$ stayed nearly constant. Increasing $N_R$ in scenario $Re - LD_A - Ped$ resulted in the strongest decline in $r_{g,g}$ of all scenarios, except if $N_p = 2$, where it remained constant. For scenario $Re - LD_A - SNP$, increasing $N_R$ from 1 to 5 slightly increased long-term $\sum \Delta G$ in $C = 30$ for selection based on $TBV$, but not notably for selection based on $EBV$ (Figure 7). The $\sigma_{g,g}^2$ in $C = 0$ was not affected by $N_R$ (Figure S4A).

DISCUSSION

In plant breeding, small effective population sizes that result from a small number of population parents crucially influence the information sources contributing to $r_{g,g}$ in a single cycle of GS. For a large number of parents, $LD_A$ and pedigree relationships are the driving forces of accuracy, whereas for few parents, cosegregation between QTL and SNPs dominates. While exploitation of information from cosegregation leads to high accuracy, it is unclear how this affects persistency of $r_{g,g}$ across selection cycles. Moreover, genetic gain depends on the available genetic variance, which is expected to be reduced for a small number of parents, as opposed to the trend expected for $r_{g,g}$. Although persistency and genetic gain in GS have been previously studied, the important
situation of the very small effective population sizes in plant breeding, where cosegregation plays a central role, has not been addressed. Hence, the purpose of the present study was to investigate the contributions of the information sources to persistency of $\rho_{g}^*$ and genetic gain across multiple cycles of recurrent GS in synthetic populations, depending on the number of parents.

**Persistency of prediction accuracy across cycles**

The persistency of $\rho_{g}^*$ in GS is of crucial importance for practical breeding, because it determines the number of generations that can be employed until retraining of the prediction equation becomes necessary. Thus, it affects the optimum design of a breeding program using recurrent GS and its costs and efficiency compared to phenotypic RS. In agreement with previous studies, we observed a substantial drop in $\rho_{g}^*$ in scenario $\text{Re-LDA-Ped}$, especially after the first cycle (Figure 4).

It was hypothesized that this decline is due to a loss of information from pedigree relationships captured by SNPs (Habier et al. 2007; Wolc et al. 2011b, 2016). In support of this explanation, we observed $\rho_{g}^*$ to plummet after the first cycle in scenario $\text{Re-LDA-SNP}$ and this can be attributed to two reasons. First, even without directional selection, the variation in pedigree relationships between the TS and RSC erodes as the number of generations between both increases (Figure S5C, selection based on RBV). Second, selection based on pedigree relationships favors the choice of candidates closely related to one another (Quinton et al. 1992; Daetwyler et al. 2007), as verified by the substantial increase in inbreeding and the reduced variation in pedigree relationships (Figure S5, A and C), making the breeding population already genetically narrow after only one selection cycle. This causes EBVs to be more similar to each other and hence, also $\rho_{g}^*$ is severely reduced, although the top pedigree relationships...
between the TS and RSC individuals increase (Figure S5B). Conversely, selection on TBV (corresponding to polygenic selection with \( h^2 = 1 \)) imposes less inbreeding (Figure S5A), because candidates can have equally high breeding values without necessarily being closely related, which results in the selection of clusters of closely related candidates (Figure S8).

The strong drop of \( r_{g\delta} \) in scenario Re \(-\) LD\(_A\) \(-\) Ped for selection based on EBV might suggest that pedigree relationships only contribute for one or at least very few generations to \( r_{g\delta} \) of scenario Re \(-\) LD\(_A\) \(-\) SNP. However, it has to be taken into account that cosegregation of SNPs and QTL allows capturing of Mendelian sampling (Daetwyler et al. 2007), which reduces the selection pressure on pedigree relationships and in turn increases persistency of \( r_{g\delta} \) in scenario Re \(-\) LD\(_A\) \(-\) SNP. The effect of reduced selection pressure on pedigree relationships can be inferred from scenario Re \(-\) LD\(_A\) \(-\) Ped under selection based on RBV, where essentially all selection pressure was removed and individuals were selected irrespective of their ancestry. Here, \( r_{g\delta} \) showed a much slower decay compared to selection based on EBV (Figure 4). This suggests that in scenario Re \(-\) LD\(_A\) \(-\) SNP with selection based on EBV, pedigree relationships probably contribute longer to \( r_{g\delta} \) than indicated by Re \(-\) LD\(_A\) \(-\) Ped (selection based on EBV).

It was previously shown that information from LD\(_A\) is highly persistent across generations (Habier et al. 2007). In synthetics, the observed LD largely corresponds to LD\(_A\) only if \( N_p \) is large, which implies that LD\(_A\) mainly contributes to \( r_{g\delta} \) for large \( N_p \) (Schopp et al. 2017). Consistent with these findings, for large \( N_p \) (e.g., 16) LD\(_A\) was the dominant information source across selection cycles, as verified by the strong reduction in \( r_{g\delta} \) when LD\(_A\) was artificially removed from scenario Re \(-\) LD\(_A\) \(-\) SNP as in Re \(-\) LE\(_A\) \(-\) SNP (Figure 4). Conversely, for small \( N_p \), the representation of LD\(_A\) in the synthetics is hampered by randomly created sample LD when selecting the parents, which raises the question how this influences persistency of \( r_{g\delta} \) for small \( N_p \). Our results show that for \( N_p = 4 \), the persistency of \( r_{g\delta} \) in scenario Re \(-\) LD\(_A\) \(-\) SNP was even higher than compared with \( N_p = 16 \) where it decreased more strongly, even though the contribution of LD\(_A\) was markedly reduced (the drop of \( r_{g\delta} \) in scenario Re \(-\) LE\(_A\) \(-\) SNP was larger for \( N_p = 4 \) than \( N_p = 16 \)) compared to \( N_p = 16 \). This implies that sample LD and therefore information from cosegregation behaves similarly to LD\(_A\) regarding the decay of information across selection cycles. The strong conservation of LD\(_A\) can be directly assessed from scenario Un \(-\) LD\(_A\) \(-\) SNP, where TS and RSC are unrelated and LD\(_A\) was the only information source (Figure 4). Here, the decay of \( r_{g\delta} \) was generally small, and if selection was based on RBV it was even diminutive, indicating that recombination between QTL and SNPs only marginally drives ancestral LD structures of the TS and the RSC apart. Even if cosegregation information dominates over LD\(_A\) in the case of small \( N_p \) (e.g., 4), LD\(_A\) still substantially contributes to \( r_{g\delta} \), especially in later selection cycles (Figure 4, Re \(-\) LD\(_A\) \(-\) SNP vs. Re \(-\) LE\(_A\) \(-\) SNP).

The genomic prediction methodology used can also have a bearing on the exploitation of the sources of information, which was not considered in this study. Previous research indicated that (Bayesian) variable selection methods are better suited to capture information from LD\(_A\) compared to GBLUP, especially if traits are oligogenic and individual QTL have strong effects (Habier et al. 2007, 2013; Zhong et al. 2009). Therefore, we expect that such methods are advantageous in situations where \( r_{g\delta} \) heavily relies on information from LD\(_A\), as is the case for large \( N_p \) or if TS and RSC are unrelated.
steady state cumulative genetic gain

In any population advanced by RS, the cumulative increase in overall performance is of central interest to breeders. Here, we continued RS until cycle $C = 30$, where further increases in $\sum \Delta G$ were only marginal because either $\sigma^2_A$ was depleted (Figure S6) and/or $r_g$ was near zero (Figure 4). This approach allowed for direct comparisons between $\sum \Delta G$ for different scenarios and conclusions were not contingent on the amount of $\sigma^2_A$ left.

Increasing $N_p$ leads to an asymptotic increase in the initially available $\sigma^2_A$, which was independent of the ancestral population in our simulation (Figure S7). According to the breeder’s equation, increasing $\sigma^2_A$ results in higher genetic gain, which partially explains the increase in $\sum \Delta G$ for larger $N_p$. However, besides higher $\sigma^2_A$, differential contributions of the three sources of information to $r_g$ play a major role. In scenario $Re - LD_A - Ped$, $\sum \Delta G$ was relatively constant from medium $N_p \geq 8$ on (Figure 3), which is presumably the result of the counterbalancing effects of a slight increase in $\sigma^2_A$ and a moderate decrease in $r_g$ with increasing $N_p$. As pointed out by Schopp et al. (2017), increasing $N_p$ from medium to large values decreases the frequency of close relatives between $T S$ and $R S C$ and hence, reduces $r_g$ (Figure S3). The contribution of pedigree relationships to long-term genetic gain in scenario $Re - LD_A - SNP$ should therefore be relatively constant for medium to large $N_p$. As the contribution of cosegregation to $r_g$ decreases with larger $N_p$, $\sum \Delta G$ of scenario $Re - LE_A - SNP$ strongly declined. Conversely, $\sum \Delta G$ of scenario $Un - LD_A - SNP$ strongly increased with larger $N_p$ due to more information from $LD_A$. Given that there is sufficient $LD_A$ present in the ancestral population ($LR$), both effects largely compensate for each other and hence, $\sum \Delta G$ in scenario $Re - LD_A - SNP$ appears to be insensitive to changes in $N_p$ beyond four parents for $LR$ (Figure 3). When there is not sufficient $LD_A$ as applies to $SR$, increasing information due to $LD_A$ can no longer compensate for the loss in cosegregation information and therefore $\sum \Delta G$ in $Re - LD_A - SNP$ decreased for higher $N_p$. Although we considered $\sum \Delta G$ close to its steady state, it is important to note that the essential trends in $\sum \Delta G$ are already apparent for as few as two selection cycles (Figure S2), which implies that our observations do not only apply to the situation of extreme long-term selection without retraining, but also to few selection cycles.

influence of $TS$ size and SNP density

We found that increasing $N_{TS}$ leads to higher persistency of $r_g$ in early selection cycles for scenarios with pedigree relationship between $T S$ and $R S C$ ($PTS = Ped$, Figure 5). This is because, for a given $N_p$, increasing $N_{TS}$ enhances the probability of obtaining $TS$ individuals that share an exceptionally large portion of their genome with the $R S C$ individuals due to Mendelian sampling and because of similarities between individuals due to $LD_A$. Hence, for small $N_{TS}$ there is a higher reliance on information from pedigree relationships (Jannink et al. 2010; Schopp et al. 2017) that quickly erodes under directional selection. For large $N_{TS}$, there is a higher weight on information from cosegregation and $LD_A$, which in turn increases the persistency of $r_g$. This shift in emphasis also entails reduced inbreeding, especially in early selection cycles (results not shown), in agreement with the findings of Jannink (2010). Therefore, if a prediction equation is to be used for multiple cycles, $N_{TS}$ should be chosen large enough to not only guarantee high initial $r_g$, but also high persistency of $r_g$ and reduced inbreeding in order to improve genetic gain from GS. Increasing SNP density from 0.125 to 2.5 $cm^{-1}$, corresponding to ~250 and 5000 SNPs in the case of maize, led to an increase in the persistency of $r_g$ (Figure 5), which is in concordance with previous studies (Solberg et al. 2009; Sonesson and Meuwissen 2009). Higher SNP density theoretically affects all three sources of information, but its influence should be strongest on $LD_A$ and cosegregation because they rely on physical proximity of SNPs and QTL. If the SNP density is extremely low (e.g., 0.125 $cm^{-1}$), it is unlikely that SNPs and QTL are tightly linked and hence, SNPs mainly capture pedigree relationships, whereas $LD_A$ and cosegregation play only subordinate roles. Therefore, high SNP density improves persistency of $r_g$ over generations, because information from both $LD_A$ (Figure 5, $N_p = 16$) and cosegregation (Figure 5, $N_p = 2$) are less prone to decay, compared to pedigree relationships. The highest SNP density we investigated was 2.5 $cm^{-1}$, which is relatively low compared to what is nowadays available in many plant species. However, because of the strong influence of cosegregation in synthetics that are produced from a low to intermediate number of parents, we would expect that little can be gained by further increasing SNP density, especially if long-range $LD_A$ is present, as can be assumed for elite germplasm in practical applications. However, the situation can be quite different for large $N_p$ and if there is only short-range $LD_A$ in the ancestral population, which rapidly increases the need for higher SNP densities.

influence of the number of recombination generations

We hypothesized that larger $N_p$ might lead to enhanced long-term $\sum \Delta G$ by virtue of a stronger fragmentation of chromosomes in the synthetic. Actually, the average length of chromosomal segments of unique parental origin decreased from ~66 cM for $N_p = 1$ to 30 cM ($N_p = 2$) and 20 cM ($N_p = 16$) for $N_p = 5$ (Figure S4B). However, as
information from pedigree relationships strongly declined with increasing \( N_p \) (Figure 6, scenario \( Re - LD_A - Ped \)), \( r_{g g} \) in \( C = 0 \) generally decreased in scenario \( Un - LD_A - SNP \). Conversely, the decline of information contributed by \( LD_A \) with increasing \( N_p \) was negligible (scenario \( Un - LD_A - SNP \)). Decreasing selection accuracy reduces \( \sum \Delta G \), which can conceal the positive effect of higher genome fragmentation. Analysis of the latter factor alone is possible with selection regime \( TBV \), where selection accuracy was always constant and equal to one, regardless of \( N_p \). Here, we found higher \( \sum \Delta G \) for \( N_p = 5 \) compared to \( N_p = 1 \) (Figure 7) because finer fragmentation promotes occurrence of genotypes with favorable allele combinations for selection. This is accompanied by a reduced coselection of QTL, such that more QTL stay polymorphic and therefore \( \sigma^2_A \) remains higher in advanced selection cycles. The positive effect of \( N_p \) on \( \sum \Delta G \) under selection on \( TBV \) increased with increasing \( N_p \), presumably because larger \( N_p \) results in even finer genome fragmentation (Figure S4B). For selection regime \( EBV \), \( \sum \Delta G \) in \( C = 30 \) was not higher for \( N_p = 5 \) than for \( N_p = 1 \), suggesting that positive and negative effects of recombination cancelled out each other. For ancestral population \( SR \), \( \sum \Delta G \) was even slightly lower for \( N_p = 5 \), because compared to \( LR \), stochastic dependency between QTL is relatively low from the beginning and hence, higher fragmentation has only a minor effect. A special situation existed for \( N_p = 2 \), which is explained in File S1.

It is noteworthy that in our simulations the initial \( \sigma^2_A \) \( (C = 0) \) was unaffected by \( N_p \), although strong sample LD between QTL was broken up. In reality, ancestral populations (corresponding to source germplasms in breeding) generally underwent some sort of directional selection, which can theoretically cause a reduction in \( \sigma^2_A \) due to the Bulmer effect (Bulmer 1971; Long et al. 2011). This hidden part of \( \sigma^2_A \) attributable to negative LD between causal loci can be recovered by recombination, which might lead to an increase in \( \sum \Delta G \) for \( N_p > 1 \).

**Implications for practical applications**

At the start of any breeding program employing GS with the goal of improving quantitative traits, breeders have to make a number of crucial decisions, including the source germplasm, parents, and mating scheme used to develop the breeding population. Further decisions specific to GS concern the \( N_{TS} \) and marker density. All of these factors influence the importance of the three information sources in GS and thereby have ramifications on the success of the breeding program.

The choice of the source germplasm crucially determines the improvement potential for the target trait (Fountain and Hallauer 1996), because it determines the genetic diversity and linkage disequilibrium (i.e., \( LD_A \)), which are both of central importance for the success of GS. Our study demonstrates that information from \( LD_A \) generally offers high persistency across selection cycles in synthetics, irrespective of \( N_p \). Hence, \( LD_A \) is particularly important for ensuring sustained genetic progress during the breeding program. However, the contribution of \( LD_A \) to genetic gain is itself highly dependent on \( N_p \). Whereas for large \( N_p \), LD in synthetics adequately represents \( LD_A \), small \( N_p \) generates sample LD and, in turn, cosegregation that dominates LD in synthetics. Cosegregation has a similarly high persistency as \( LD_A \), but it can only contribute to genetic gain if \( TS \) and selection candidates are related by having parents in common. However, it must be taken into account that reducing \( N_p \) also reduces the initially available genetic variance for breeding, thereby impairing \( \sum \Delta G \). In essence, high persistency of \( r_{g g} \) and thereby prolonged genetic progress may be achieved irrespective of \( N_p \), but if \( N_p \) is large, substantial \( LD_A \) is required.

Pedigree relationships also contribute to predictive information for \( N_p > 2 \), and harnessing pedigree information has been recommended to achieve high \( r_{g g} \) in GS (e.g., Wricke et al. 2011a). Frequent retraining of the prediction equation, at best in every generation, would be required to optimally exploit pedigree relationships because information from them rapidly erodes over generations, especially under directional selection. In addition, selection using pedigree relationships increases the rate of inbreeding due to intraclass correlation of EBV for members of the same family and their coselection (Daetwyler et al. 2007), a result that is well known in animal breeding (Belonsky and Kennedy 1988) and was confirmed in our study for synthetics in plant breeding (Figure S5A). A high rate of inbreeding is undesirable in long-term selection, because genetic diversity is rapidly depleted and eventually \( \sum \Delta G \) is compromised. In GS, it was shown that molecular markers not only capture deviations of genomic relationships from pedigree relationships, but also the pedigree relationships themselves (Habier et al. 2007), i.e., the latent family structure in the case of synthetics. Therefore, the same concerns as for pedigree-based selection partially apply to GS, so that GS is also prone to selection of close relatives and inbreeding (Jannink 2010). If the breeding objective is long-term \( \sum \Delta G \), as classically targeted by RS in genetically broad-based populations (Hallauer and Carena 2012), corresponding to large \( N_p \) in our study, deliberate avoidance of using pedigree relationships might be desirable for maximizing long-term \( \sum \Delta G \).

There are different possibilities to reduce the influence of pedigree relationships. Increasing both \( N_{TS} \) and marker density leads to an improved capturing of Mendelian sampling and
similarities between individuals due to $L_{D_{1}}$, which reduces the reliance on pedigree relationships and in turn reduces inbreeding. Another possibility could be modeling information from $L_{D_{2}}$, cosegregation (Calus et al. 2008; Legarra and Fernando 2009), and pedigree relationships in a joint linear mixed model in an attempt to isolate information from pedigree relationships. Alternatively, one could modify the mating scheme used for generating the synthetic. Additional generations of recombination successfully decreased strong variation in pedigree relationships between individuals, but only up to $N_{r} \leq 5$ where a baseline level was reached (Figure S4C). Mating schemes as employed for establishing the Multi-parent Advanced Generation Inter­crosses (MAGIC) largely avoid population substructure and pedigree relationships, while they complement the favorable properties of synthetics such as high genetic diversity and elevated minor allele frequencies with a fine-grained mosaic of the genome (compare Dell’Acqua et al. 2015; Holland 2015). Thus, they potentially represent ideal candidates for long-term recurrent GS, but this warrants further research.

ACKNOWLEDGMENTS
This study was financially supported by the project “Climate Resilient Maize for ASIA (CRMA)” from the International Maize and Wheat Improvement Center, México and the Deutsche Gesellschaft für Internationale Zusammenarbeit, project no. 15.7860.8-001.00 (contract no. 81194991).

LITERATURE CITED
Bastiaansen, J. W. M., A. Coster, M. P. L. Calus, J. A. M. van Arendonk, and H. Bovenhuis, 2012 Long-term response to genomic selection: effects of estimation method and reference population structure for different genetic architectures. Genet. Sel. Evol. 44: 3.
Belonsky, G. M., and B. W. Kennedy, 1988 Selection on individual phenotype and best linear unbiased predictor of breeding value in a closed swine herd. J. Anim. Sci. 66: 1124-1131.
Bernardo, R., 2009 Should maize doubled haploids be induced among F1 or F2 plants? Theor. Appl. Genet. 119: 255-262.
Bernardo, R., and J. Yu, 2007 Prospects for genomewide selection for quantitative traits in maize. Crop Sci. 47: 1082-1090.
Beyene, Y., K. Semagn, S. Mugo, A. Tarekegne, R. Babu et al., 2015 Genetic gains in grain yield through genomic selection in eight bi-parental maize populations under drought stress. Crop Sci. 55: 154-163.
Bulmer, M. G., 1971 The effect of selection on genetic variability. Am. Nat. 105: 201-211.
Calus, M. P. L., T. H. E. Meuwissen, A. P. W. de Roos, and R. F. Veerkamp, 2008 Accuracy of genomic selection using different methods to define haplotypes. Genetics 178: 553-561.
Coster, A., 2013 Pedigree: Pedigree Functions. Available at: https://rdrr.io/cran/pedigree. Accessed: Month day, year.
Daetwyler, H. D., B. Villanueva, P. Bijma, and J. A. Woolliams, 2007 Inbreeding in genomewide selection. J. Anim. Breed. Genet. 124: 369-376.
Daetwyler, H. D., B. Villanueva, and J. A. Woolliams, 2008 Accuracy of predicting the genetic risk of disease using a genome-wide approach. PLoS One 3: e3995.
Dell’Acqua, M., D. M. Gatti, G. Pea, F. Cattonaro, F. Coppens et al., 2015 Genetic properties of the MAGIC maize population: a new platform for high definition QTL mapping in Zea mays. Genome Biol. 16: 167.
Endelman, J. B., 2011 Ridge regression and other kernels for genomic selection with R package rrBLUP. Plant Genome J. 4: 250.
Falconer, D. S., and T. F. C. Mackay, 1996 Introduction to Quantitative Genetics. Benjamin Cummings, San Francisco.
Fountain, M. O., and A. R. Hallauer, 1996 Genetic variation within maize breeding populations. Crop Sci. 36: 26-32.
Goddard, M., 2009 Genomic selection: prediction of accuracy and maximisation of long term response. Genetica 136: 245-257.
Goddard, M. E., B. J. Hayes, and T. H. E. Meuwissen, 2011 Using the genomic relationship matrix to predict the accuracy of genomic selection. J. Anim. Breed. Genet. 128: 409-421.
Gorjanc, G., J. Jenko, S. J. Hearne, and J. M. Hickey, 2016 Initiating maize pre-breeding programs using genomic selection to harness polygenic variation from landrace populations. BMC Genomics 17: 30.
Habier, D., R. L. Fernando, and J. C. M. Dekkers, 2007 The impact of genetic relationship information on genome-assisted breeding values. Genetics 177: 2389-2397.
Habier, D., J. Tetens, F.-R. Seefried, P. Lichtner, and G. Thaller, 2010 The impact of genetic relationship information on genomic breeding values in German Holstein cattle. Genet. Sel. Evol. 42: 5.
Habier, D., R. L. Fernando, and D. J. Garrick, 2013 Genomic BLUP decoded: a look into the black box of genomic prediction. Genetics 194: 597-607.
Hallauer, A. R., 1992 Recurrent selection in maize. Plant Breed. Rev. 9: 115-179.
Hallauer, A. R., and M. J. Carena, 2012 Recurrent selection methods to improve germplasm in maize. Maydica 57: 266-283.
Hayes, B. J., P. M. Visscher, and M. E. Goddard, 2009 Increased accuracy of artificial selection using the realized relationship matrix. Genet. Res. 91: 47-60.
Heffner, E. L., A. J. Lorenz, J. L. Jannink, and M. E. Sorrels, 2010 Plant breeding with genomic selection: gain per unit time and cost. Crop Sci. 50: 1681-1690.
Holland, J. B., 2015 MAGIC maize: a new resource for plant genetics. Genome Biol. 16: 163.
Jannink, J.-L., 2010 Dynamics of long-term genomic selection. Genet. Sel. Evol. 42: 35.
Jannink, J.-L., A. J. Lorenz, and H. Iwata, 2010 Genomic selection in plant breeding: from theory to practice. Brief. Funct. Genomics 9: 166-177.
Legarra, A., and R. L. Fernando, 2009 Linear models for joint association and linkage QTL mapping. Genet. Sel. Evol. 41: 43.
Liu, H., T. Meuwissen, A. C. Sørensen, and P. Berg, 2015 Upweighting rare favourable alleles increases long-term genetic gain in genomic selection programs. Genet. Sel. Evol. 47: 19.
Long, N., D. Gianola, G. J. M. Rosa, and K. A. Weigel, 2011 Marker-assisted prediction of non-additive genetic values. Genetica 139: 843-854.
Massman, J. M., H. J. G. Jung, and R. Bernardo, 2013 Genomewide selection vs. marker-assisted recurrent selection to improve grain yield and stover-quality traits for cellulosic ethanol in maize. Crop Sci. 53: 58-66.
Meuwissen, T. H. E., B. J. Hayes, and M. E. Goddard, 2001 Prediction of total genetic value using genome-wide dense marker maps. Genetics 157: 1819-1829.
Mikel, M. A., 2006 Availability and analysis of proprietary dent corn inbred lines with expired U.S. plant variety protection. Crop Sci. 46: 2555-2560.
Mikel, M. A., and J. W. Dudley, 2006 Evolution of North American dent corn from public to proprietary germplasm. Crop Sci. 46: 1193-1205.
Muir, W. M., 2007 Comparison of genomic and traditional BLUP-estimated breeding value accuracy and selection response under alternative trait and genomic parameters. J. Anim. Breed. Genet. 124: 342-355.
Nielsen, H. M., A. K. Sonesson, H. Yazdi, and T. H. E. Meuwissen, 2009 Comparison of accuracy of genome-wide and BLUP breeding value estimates in sib based aquaculture breeding schemes. Aquaculture 289: 259-264.
Quinton, M., C. Smith, and M. E. Goddard, 1992 Comparison of selection methods at the same level of inbreeding. J. Anim. Sci. 70: 1060-1067.
R Core Team, 2015 R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria.
Sargolzaei, M., and F. S. Schenkel, 2009 QMSim: a large-scale genome simulator for livestock. Bioinformatics 25: 680-681.
Schnable, P. S., X. Xu, L. Civardi, Y. Xia, A.-P. Hsing et al., 1996 The role of meiotic recombination in generating novel genetic variability, pp. 103-110 in The Impact of Plant Molecular Genetics, edited by Sobral, B. W. S. Birkhäuser, Boston, MA.
Schopp, P., D. Müller, F. Technow, and A. E. Melchinger, 2017  Accuracy of genomic prediction in synthetic populations depending on the number of parents, relatedness and ancestral linkage disequilibrium. Genetics 205: 441-454.

Solberg, T. R., and A. K. Sonesson, J. A. Woolliams, J. Odegard, and Meuwissen, T. H. E., 2009  Persistence of accuracy of genome-wide breeding values over generations when including a polygenic effect. Genet. Sel. Evol. 41: 53.

Sonesson, A. K., and T. H. E. Meuwissen, 2009  Testing strategies for genomic selection in aquaculture breeding programs. Genet. Sel. Evol. 41: 37.

Van Grevenhof, E. M., J. A. Van Arendonk, and P. Bijma, 2012  Response to genomic selection: the Bulmer effect and the potential of genomic selection when the number of phenotypic records is limiting. Genet. Sel. Evol. 44: 26.

VanRaden, P. M., 2008  Efficient methods to compute genomic predictions. J. Dairy Sci. 91: 4414-4423.

Windhausen, V. S., G. N. Atlin, J. M. Hickey, J. Crossa, J.-L. Jannink et al., 2012  Effectiveness of genomic prediction of maize hybrid performance in different breeding populations and environments. G3 2: 1427-1436.

Wolc, A., J. Arango, P. Settar, J. E. Fulton, N. P. O’Sullivan et al., 2011a  Persistence of accuracy of genomic estimated breeding values over generations in layer chickens. Genet. Sel. Evol. 43: 23.

Wolc, A., C. Stricker, J. Arango, P. Settar, J. E. Fulton et al., 2011b  Breeding value prediction for production traits in layer chickens using pedigree or genomic relationships in a reduced animal model. Genet. Sel. Evol. 43: 5.

Wolc, A., J. Arango, P. Settar, J. E. Fulton, N. P. O’Sullivan et al., 2016  Mixture models detect large effect QTL better than GBLUP and result in more accurate and persistent predictions. J. Anim. Sci. Biotechnol. 7: 7.

Yabe, S., R. Ohsawa, and H. Iwata, 2013  Potential of genomic selection for mass selection breeding in annual allogamous crops. Crop Sci. 53: 95-105.

Yabe, S., M. Yamasaki, K. Ebana, T. Hayashi, and H. Iwata, 2016  Island-model genomic selection for long-term genetic improvement of autogamous crops. PLoS One 11(4): e0153945.

Zhong, S., J. C. M. Dekkers, R. L. Fernando, and J.-L. Jannink, 2009  Factors affecting accuracy from genomic selection in populations derived from multiple inbred lines: a Barley case study. Genetics 182: 355-364.

Communicating editor: J. B. Holland