Genome-wide prediction of hybrid performance and yield stability analysis in winter wheat

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1. General introduction

Wheat (*Triticum aestivum* L.) is one of the most widely grown crops, occupying 17 percent of the total arable land in the world (Reynolds et al. 2011). As a consequence of adopting Green Revolution technologies, a linear increase in the production of wheat has been achieved since the early 1960s (Evenson and Gollin 2003). Such rapid improvement relies on improved varieties, expansion of irrigation, and the widespread use of fertilizers (Whitford et al. 2013). To meet the expected demand of food, feed, and biofuel by 2050, wheat production must be doubled (Tilman et al. 2011). Unfortunately, the potential of expanding the cultivated area, as well as area under irrigation or increasing fertilizer usage is limited. Therefore, wheat production must be primarily increased by enhancing yields per unit area under cultivation. Yield growth in wheat through line breeding, however, has stagnated in several parts of the world (Ray et al. 2012). Hybrid breeding is considered as a promising alternative to boost yield per unit area and enhance yield stability in ever-changing climates (Zhao et al. 2015a).

Hybrid breeding in wheat

The phenomenon, that progenies produced by crossing pure inbred lines show an increase of characters that previously suffered an inhibition from inbreeding, is termed as “hybrid vigor” or “heterosis” (Falconer and Mackay 1996). Heterosis was first described in the 18th century but the term was later coined by Shull (1914). The first commercial hybrid variety was marketed for *Begonia semperflorens* as early as 1910 in Germany (Wricke and Weber 1986). The enormous economic importance of hybrid varieties was revealed by the commercial adoption of hybrid maize varieties in the United States of America in the 1930s (Duvick 2005). Hybrid maize became widely grown, occupying 50% of maize area by 1943 and 100% by 1960, while the mean yields increased sharply from less than 2 Mg ha^{-1} in 1930 to 4 Mg ha^{-1} in 1960 (Bernardo 2002).

Another important reason for the rapid spread of hybrids was that crop production was more reliable for hybrids compared to open-pollinated cultivars (Bernardo 2002).

The success of hybrid maize stimulated the interest in hybrid wheat (Wilson and Driscoll 1983). However, early attempts failed to realize an efficient and cost-efficient hybrid seed production by inducing male sterility via mechanical and chemical approaches (Lelley 1976). The discovery of cytoplasmic male sterility (CMS) and male-fertility restoration in wheat again stimulated research on hybrid wheat. The first commercial hybrid wheat variety based on a CMS system was marketed in the U.S.A. in the 1970s and the first commercial hybrid wheat variety using chemical hybridizing agent (CHA) was registered in 1985 (Edwards 2001). Although intensive work on hybrid wheat has been researched for several decades, hybrid wheat accounts for a marginal fraction of the total wheat area and no efficient and cost effective hybrid production system has been established so far for commercial use (Longin et al. 2012; Whitford et al. 2013).

A cost-efficient hybrid seed production system is one of the prerequisites for successful implementation of hybrid breeding (Dreisigacker et al. 2005). The most efficient approach to facilitate cross-pollination in bisexual plants is to obtain male sterility (Kempe et al. 2014). Several different methods to achieve male sterility exist, among which the easiest is to sterilize the male organ of the female parent by removing the anthers (Smith et al. 2004). However, the ‘detasseling’ method is laborious, time-consuming, and expensive for crops that do not have a physical separation of male and female flower organs, and is usually not viable as a production method. For wheat, the common strategies for hybrid production are to use (1) a CMS system, (2) gametocides, or (3) transgenic technology; but all of these strategies currently have mitigating factors. CMS is based on mutated mitochondrial DNA and nuclear DNA and is achieved only when the two mutations are present in the same plant (Schnable and Wise 1998). The male fertility can be restored by nuclear fertility restoring genes, which are specific to each CMS system (Chase 2007). CMS is successfully exploited in some cereals, such as rice, but in wheat CMS is difficult to develop, maintain, and especially restore (Kempe et al. 2014). CHAs are gametocytes that are common for hybrid production in the European wheat market (Edwards 2001). However, the application of CHAs is hampered by several problems, including expense, compromised seed production, and sensitivity to growth stage and environmental factors. Genetic modification technologies also can be adopted to induce male-sterility (Kempe and Gils 2011) but these technologies are not well accepted in several parts of the world, and therefore are hindered for political and sociological reasons. Consequently, further efforts are required to establish an efficient and cost-effective hybridization system for wheat.

With the exploitation of heterosis, hybrid wheat is expected to show higher yield performance than lines per se. Many studies have investigated the amount and range of heterosis for grain yield using both CMS- and CHA-based wheat hybrids (Barbosa-Neto et al. 1996; Corbellini et al. 2002; Longin et al. 2013; Oury et al. 2000; Perenzin et al. 1998). The average heterosis for grain yield was around 10% in wheat resulting in yield advantages of up to 1.0 Mg ha^{-1} for hybrids compared to best commercial varieties (Gowda et al. 2012; Zhao et al. 2015a). Thus, hybrid breeding has the potential to outperform line variety breeding in wheat.

Yield stability

Yield stability reflects how well a candidate germplasm performs across different environments and is an important trait for both breeders and growers. Yield performance is the consequence of genetic and non-genetic effects during the growing and grain-filling periods, which includes a number of physiological and biochemical responses (Ceccarelli et al. 1991). Therefore, yield stability is the complex result of the reaction of a genotype's yield performance to varying environmental factors. Yield stability is assessed with various biometrical approaches. Several yield stability parameters have been put forward which were classified as either static or dynamic concepts of stability (Becker and Léon 1988).

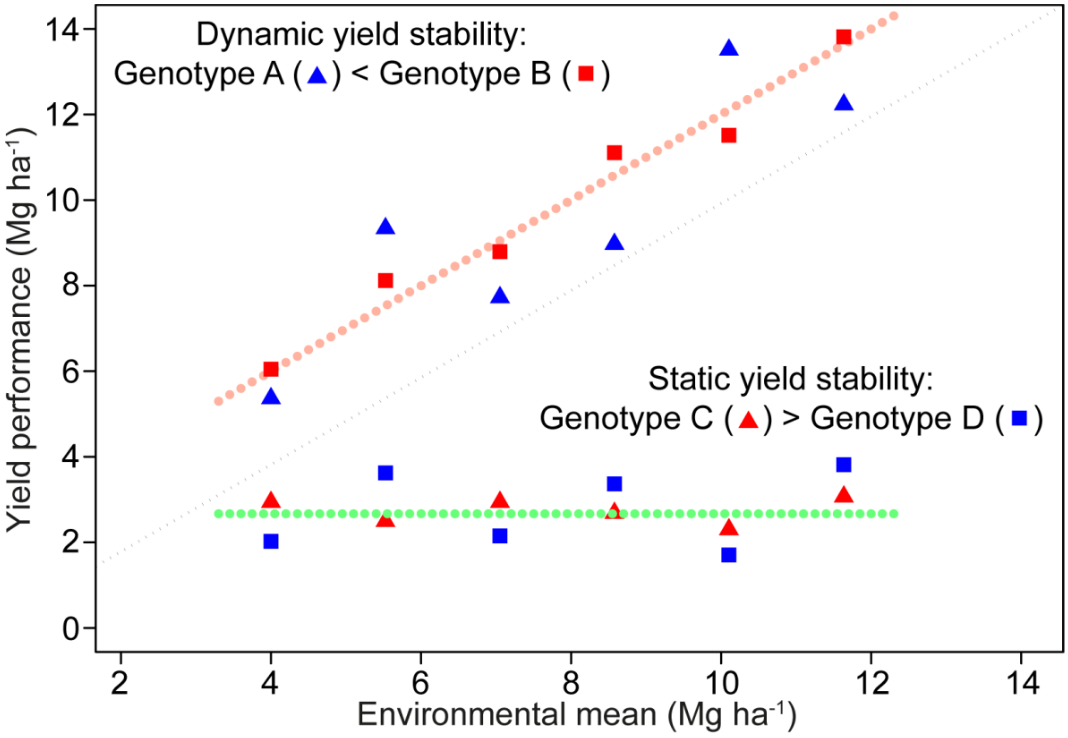

Figure 1. Exemplary description of yield stability

According to the static concept of stability, varieties that show constant performance across different environments are stable (**Figure 1**). Static stability can be estimated using Finlay-Wilkinson (Finlay and Wilkinson 1963) or Eberhart-Russell regression models (Eberhart and Russell 1966). Both models are based on regressing individual performances on the environmental means. Genotypes that are stable under a static concept would in many cases neglect favorable environmental conditions. Therefore, static yield stability is frequently associated with low yield performance and of low economic relevance (Becker and Léon 1988; Lin et al. 1986). Nevertheless, the static concept of stability is valuable for traits that aim to maintain a certain level of performance across growing conditions; for instance, quality traits and traits of resistance to biotic and abiotic stress (Becker and Léon 1988). In the dynamic stability concept, changes in performance of a genotype are consistent with the changes of average performance of all genotypes across environments (Figure 1; Mühleisen et al. 2014b). The most popular approach for estimation of the dynamic stability is to calculate genotype-specific genotype-by-environment interaction variances (Shukla 1972; Wricke 1962).

Table 1. Studies investigating yield stability parameters of hybrids and lines in wheat

NE	NH	NL	Parameters	Outcome	Reference
3	10	11	Deviation variance	Hybrid superior	(Borghi et al. 1988)
~20	4-6	37-45	Deviation variance	Similar	(Peterson et al. 1997)
3	311	59	Geno-by-Env interaction variance	Hybrid superior	(Oury et al. 2000)
~10	1-17	3-22	Eberhart-Russell regression	Similar	(Koemel et al. 2004)
5	40	16	Geno-by-Env interaction variance	Hybrid superior	(Gowda et al. 2010)
5	1604	135	Shukla’s stability	Hybrid superior	(Mühleisen et al. 2014a)

NE, NH, and NL represent number of environments, number of hybrids, and number of lines, respectively.

Hybrids are expected to display higher yield stability due to buffering effects caused by integrated genetic constitution (Hallauer et al. 1988). Comparison between the yield stability of hybrids and lines can be achieved by contrasting the means of both groups or by comparing the performance of individual genotypes. Studies on yield stability for hybrids versus lines in wheat revealed contrasting results (Table 1), varying from similar yield stability (Koemel et al. 2004; Peterson et al. 1997) to hybrid superiority (Borghi et al. 1988; Gowda et al. 2010; Mühleisen et al. 2014a; Oury et al. 2000). Most previous studies were performed either based on a limited number of field trials or group-based yield stability parameters. Assessment of yield stability parameters of individual genotypes requires intensive phenotyping in many environments (Mühleisen et al. 2014b). Yield stability research based on individual genotypes has not been done yet in wheat with appropriate phenotyping intensity.

Heritability is a central parameter to judge the quality of yield stability measures and to infer the required intensity level of phenotyping (Léon and Becker 1988; Mühleisen et al. 2014b). The heritability of yield stability was obtained by correlating the results of a subset of environments with yield stability estimates of the complete set of environments (Léon and Becker 1988; Robert 2002). These estimates of heritability for yield stability, however, are biased unless the data set contains a very large number of environments. Mühleisen et al. (2014b) developed a modified heritability estimate for yield stability on the basis of correlation coefficients of stability parameters derived from two independent subsets. The drawback of this approach is that the assumption of independent residuals for both subsets could lead to biased estimates for heritability of yield stability when the assumption of independence is not true. In addition to the conventional strategy for assessing yield stability, indirect selection could be one promising approach if a genetic correlation exists between yield stability and other agronomic traits (Bernardo 2002). The potential of indirect selection for yield stability has been not yet been assessed for wheat.

Quality traits and important disease resistances in hybrid wheat breeding

Quality traits are central targets for wheat improvement (Bonjean and Angus 2001). The quality properties of wheat are tightly related to bread-making and animal-feeding and are controlled by genetic, environmental, and biochemical factors (Peterson et al. 1998). The nutritional value and baking quality of wheat is mainly reflected by the total protein content, especially the gluten proteins, which are evaluated using the sedimentation test according to Zeleny (Shewry et al.

1995). The kernel hardness, which is based on milling texture, is supposed to be related to proteins that control the adhesion of starch granules (Greenwell and Schofield 1986; Worland and Snape 2001). In addition to kernel hardness, test weight and 1000-kernel weight are also relevant indexes to portray wheat kernel composition and potential of flour extraction (Freund and Kim 2006).

Biotic stress affects the plant development and causes serious economic losses in crops. As a consequence, exploring cultivars with improved resistance to biotic stress is a primary goal of breeding programs throughout the world (Miklas et al. 2006). *Fusarium head blight* (FHB), caused by *Fusarium graminearum,* and *Septoria tritici blotch* (STB), caused by *Mycosphaerella graminicola*, are two important fungal diseases in wheat (Bonjean and Angus 2001). Occurrence of both diseases severely impacts the wheat production and quality worldwide (Miedaner et al. 2011; Miedaner et al. 2013; Mirdita et al. 2015a). Hence, increasing FHB and STB resistance are central targets for hybrid wheat breeding.

Prediction of hybrid performance

Assessing the resistance against FHB and STB, as well as quality traits is labor- and time-consuming. The difficulties in measuring phenotypic performance hampers the identification of superior hybrids and entails the need to accelerate the implementation of efficient strategies to predict hybrid performance.

Hybrid performance can be predicted based on mid-parent (MP) performance or general combining ability (GCA) effects. Predicting the hybrid performance based on mid-parent performance or general combining ability effects are accurate for traits which are mainly additively inherited. Nevertheless, both approaches require that parental lines of the tested hybrids are evaluated in the estimation set based on the per se or their hybrid performance

(Schrag et al. 2010). Therefore, MP performance and GCA prediction are restricted to closely related hybrids and useless to predict independent hybrids.

With the development of sequencing technology, genomic-assisted crop improvement became a popular approach to predict the hybrid performance. Hybrid prediction can be performed either using marker-assisted selection (MAS; Lande and Thompson 1990) or genomic selection (GS; Meuwissen et al. 2001). The procedures of both strategies are similar, requiring a phenotyped and genotyped training population and a genotyped test population (**Figure 2**). The most obvious difference is the marker resource in the test population: Prediction of genotypic values by MAS is based on the effects of a limited number of selected markers that show significant marker-trait association. In contrast, in GS all markers are used without marker-specific significance test (Heffner et al. 2009; Zhao et al. 2015b). MAS is most effective for traits that are controlled by a few major genes and GS is preferable if the genetic architecture of target traits is complex (Heffner et al. 2009; Heslot et al. 2012).

Several quantitative trait loci (QTL) that exhibit large effects have been reported for kernel hardness and gluten content in the past decades (Giroux and Morris 1998; Singh and Shepherd 1985). Nevertheless, such large effect QTL are often already fixed in the elite breeding programs (Groos et al. 2004). Quite a lot of studies were conducted to detect potential large effect QTL underlying resistance against FHB and STB, as well as quality traits (Table 2), but so far no stable QTL were reported, indicating their complex genetic architecture. To cope with their complex genetic architecture, GS, which considers many markers without marker-specific tests (Heffner et al. 2009; Zhao et al. 2015b), offers a promissing approach for hybrid prediction. The potential of MAS for predicting the hybrid performance of resistance against FHB and STB, as well as quality traits has not yet been investigated.

Table 2. Genome-wide association studies on disease resistance and quality traits in wheat

Traits	Population type	Population size	Method	Reference
STB	Hybrid	1142	GWAS, GS	(Miedaner et al. 2013)
FHB, STB	Line	2325	GWAS, GS	(Mirdita et al. 2015a)
FHB	Line	455	GWAS	(Miedaner et al. 2011)
FHB	RIL	194	GWAS	(Gervais et al. 2003)
Prot, TKW	Line	376	GWAS, GS	(Bentley et al. 2014)
Hard, Prot, SDS, TEW, TKW	RIL	188	GWAS	(Carter et al. 2012)
Hard, Prot, TEW, TKG	DH	185	GWAS	(El-Feki et al. 2013)
Hard, Prot, TEW, TKG	RIL	100	GWAS	(Galande et al. 2001)
Prot, TKW	RIL	194	GWAS	(Groos et al. 2003)
Prot, SDS, TEW, TKG	DH	185	GWAS	(Huang et al. 2006)
Hard, Prot, SDS, TEW	BC	400	GWAS	(Kunert et al. 2007)
Gluten, Hard, Prot, SDS	RIL	198	GWAS	(Li et al. 2009)
Prot, SDS, Starch	DH	182	GWAS	(McCartney et al. 2006)
Prot, SDS, Starch, TEW, TKG	Line	207	GWAS	(Reif et al. 2011)
Hard, Prot, SDS, TKW	RIL	226	GWAS	(Zanetti et al. 2001)

Population type: Backcross (BC); Doubled haploid (DH); Recombinant inbred line (RIL).
Traits: *Fusarium head blight* (FHB); Gluten content (Gluten); Kernel hardness (Hard); Protein content (Prot); Sedimentation volume (SDS); *Septoria tritici blotch* (STB); Starch content (Starch); Test weight (TEW); 1000-kernel weight (TKG).
Method: Genome-wide association study (GWAS); Genomic selection (GS).

Ignoring minor effect marker in MAS and over-shrinkage of major effect marker in GS could probably limit the accuracy of prediction. Zhao et al. (2014) suggested to bridge the gap between MAS and GS using a weighted best linear unbiased prediction (W-BLUP) model, which boosted the prediction accuracy for traits that are controlled by a few large and many small effect QTL. The W-BLUP model was so far only evaluated for traits with functional markers. In case no functional markers are available, genome-wide association study should be adopted to detect significant marker-trait associations if no functional markers are available.

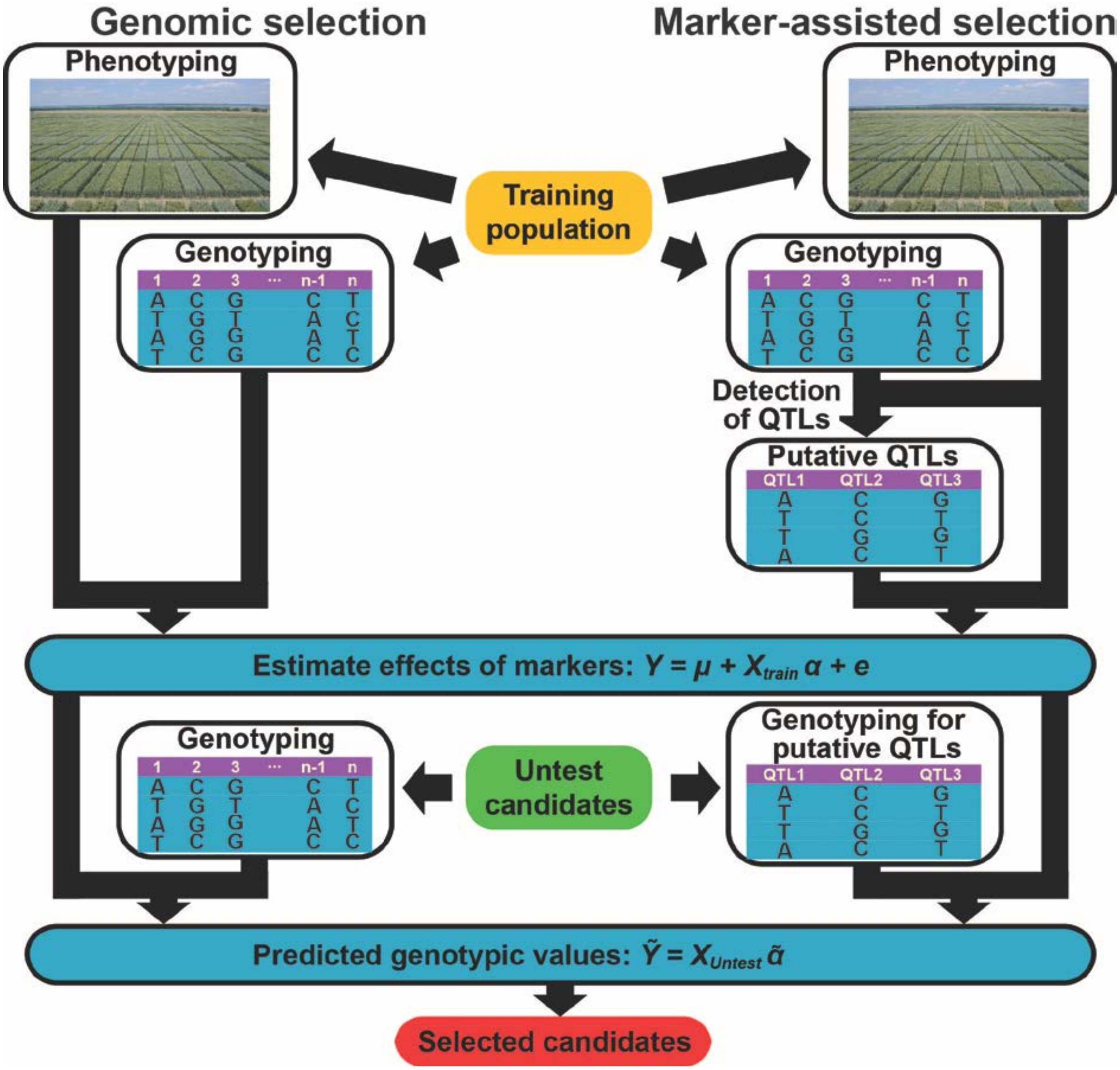

Figure 2. Procedure of marker-assisted selection and genomic selection

The comparative efficiencies of the above outlined phenotypic and genomic-assisted selection strategies depend on the annual selection gain under a constraint budget. Longin et al. (2014) reported that the advantage of GS versus field evaluation is mainly determined by the prediction accuracy of GS. Therefore, improving the prediction accuracy of GS will make it an outstanding approach as compared to phenotypic selection. The prediction accuracy of GS is reported to be controlled by the genetic architecture (Mirdita et al. 2015b) and the relatedness between test and estimation set (Gowda et al. 2014; Jiang et al. 2015), both of which are intrinsic properties that are impossible to control. Moreover, Meuwissen (2009) reported in a simulation study that the marker density and composition of estimation population also had an effect on the prediction accuracy of GS. Therefore, exploring the influence of the marker density and composition of estimation population could probably lead to maximum exploitation of the prediction accuracy of GS.

2. Objectives

The overall goals of the present thesis were to explore efficient strategies for precise assessment of yield stability and to investigate the potential and limits to predict the hybrid performance for important agronomic and quality traits in wheat. In particular, the objectives were to:

(1) develop and implement an improved heritability estimate to examine the required scale for assessing yield stability[1],

(2) compare yield performance and yield stability of hybrids and inbred lines[1],

(3) investigate the association of agronomic traits with yield stability[1],

(4) explore the possibility of selecting subsets of environments allowing to portray large proportion of variation of yield stability[1],

(5) examine the association between FHB and STB disease severities[2],

(6) investigate the genetic architecture of FHB and STB disease resistances[2],

(7) assess the potential of marker-assisted and genomic selection for improving FHB and STB disease resistances[2],

(8) examine the presence of major effect QTL for quality traits[3],

(9) explore optimal strategies for predicting hybrid performance for quality traits[3],

(10) investigate the effects of marker density and the composition and size of the training population on the accuracy of prediction of hybrid performance[3], and

(11) provide access to a wheat quality data set of a comprehensive hybrid population[4].

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[1] Liu G, Zhao Y, Mirdita V, Reif JC (2017)

Efficient strategies to assess yield stability in winter wheat.

Theoretical and applied Genetics DOI: 10.1007/s00122-017-2912-6

[2] Mirdita V, Liu G, Zhao Y, Miedaner T, Longin CFH, Gowda M, Mette MF, Reif JC (2015)

Genetic architecture is more complex for resistance to Septoria tritici blotch than to Fusarium head blight in Central European winter wheat.

BMC Genomics 16:430

[3] Liu G, Zhao Y, Gowda M, Longin CFH, Reif JC, Mette MF (2016)

Predicting hybrid performances for quality traits through genomic-assisted approaches in Central European wheat.

PLoS ONE 11(7):e0158635

[4] Liu G (2016)

Phenotypic data of seven quality traits for a population of Central European wheat hybrids and their parental inbred lines.

DOI:10.5447/IPK/2016/11.

3. Original papers

3.1 Efficient strategies to assess yield stability in winter wheat

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Theoretical and Applied Genetics DOI: 10.1007/s00122-017-2912-6

The original paper has been published in an international journal and attached in the submitted version. Due to copyright restrictions, it will be removed in the final version submitted to library.

The paper is available online:

https://rd.springer.com/article/10.1007/s00122-017-2912-6

3.2 Genetic architecture is more complex for resistance to Septoria tritici blotch than to Fusarium head blight in Central European winter wheat

Vilson Mirdita[1], Guozheng Liu[1], Yusheng Zhao[1], Thomas Miedaner, C[2]. Friedrich H. Longin[2], Manje Gowda[3], Michael Florian Mette[1], Jochen C. Reif[1]

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BMC Genomics (2015) 16: 430

The original paper has been published in an international journal and attached in the submitted version. Due to copyright restrictions, it will be removed in the final version submitted to library. The paper is available online:

https://bmcgenomics.biomedcentral.com/articles/10.1186/s12864-015-1628-8

3.3 Predicting hybrid performances for quality traits through genomic-assisted approaches in Central European wheat

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PLoS ONE (2016) 11(7): e0158635

The original paper has been published in an international journal and attached in the submitted version. Due to copyright restrictions, it will be removed in the final version submitted to library. The paper is available online:

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0158635

3.4 Phenotypic data of seven quality traits for a population of Central European wheat hybrids and their parental inbred lines

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DOI: 10.5447/IPK/2016/11

Abstract

This data resource contains the Best Linear Unbiased Estimates of 135 elite winter wheat (Triticum aestivum L.) lines adapted to Central Europe and 1,604 F1 hybrids derived from them. All genotypes were evaluated for seven quality traits in up to six environments (Zhao et al. 2015; Proceedings of the National Academy of Sciences of the United States of America 112:15624-15629; DOI: 10.1073/pnas.1514547112; Liu et al. 2016. Liu et al. 2016; PlosOne; DOI: 10.1371/journal.pone.0158635). The sedimentation (SDS) volume according to Zeleny (unit ml) providing a measure for gluten content and swelling properties and thus baking quality of wheat was determined in accordance with International Association for Cereal Science and Technology (ICC) Standards 116/1 and 118 (http://www.icc.or.at/standard_methods). Protein, gluten, and starch content (unit %) as well as hardness were determined by near infrared reflectance (NIR) spectroscopy in accordance to ICC Standard 159 (http://www.icc.or.at/standard_methods). 1000-kernel weight (unit g) and test weight (unit kg hL-1) were determined in accordance with variety registration regulations

4. General discussion and future prospects

Hybrid breeding offers the potential to boost grain yield in wheat

Hybrids generated based on chemical hybridization agents or cytoplasmic male sterility, which can reduce the yield advantage of wheat hybrids compared to a manual strategy (Allan 1973; Whitford et al. 2013), showed an average midparent heterosis of 10% (Gowda et al. 2012; Longin et al. 2013; Zhao et al. 2015a). Furthermore, wheat hybrids were considerable more resistant against biotic and abiotic stresses (Mirdita et al. 2015b; Zhao et al. 2013), which significantly reduce the expense and the risk of substantial loss of yield performance. Although further efforts are required to develop efficient hybrid seed production systems for wheat (Whitford et al. 2013), hybrid breeding seems to be a promising strategies to cope with increased demand for food, feed, and other purposes (Tilman et al. 2011). In the present thesis, two hybrid-involved data sets, i.e., official winter wheat registration trials in Germany and an experimental hybrid population, were analyzed to investigate the advantages of wheat hybrids in grain yield performance. Hybrids of both data sets were generated by applying chemical hybridization agents. The official trials consisted of five different series and each series was tested in multi-locations in three consecutive years with a maximum of 2 hybrids (**Figure 4A**). The experimental population comprised 1,604 wheat hybrids and was generated using a factorial mating design with 120 female lines and 15 male lines (**Figure 4B**). The 135 parental lines were provided by four breeding companies and reflect a diversity panel (**Figure 5**).

Zhao et al. (2015a) reported that the experimental wheat hybrids showed a yield advantage up to 1.0 Mg ha^{-1} compared to the best commercial variety. The official winter wheat registration trials confirmed this tendency and the average yield performance of hybrid candidates was significantly larger than that of elite line candidates (Liu et al. 2017). This is remarkable as the investments were much higher for line than that for hybrid breeding.

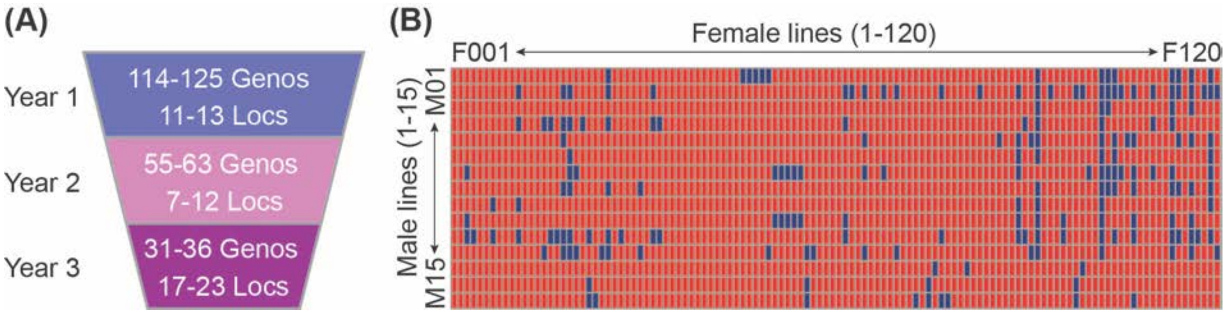

Figure 4. (A) Procedure for official winter wheat registration trials and (B) factorial mating design applied to establish the experimental hybrid population. Red cells indicate the presence and blue cells indicate the absence of hybrid combination. “Genos” and “Locs” are abbreviations for “Genotypes” and “Locations”

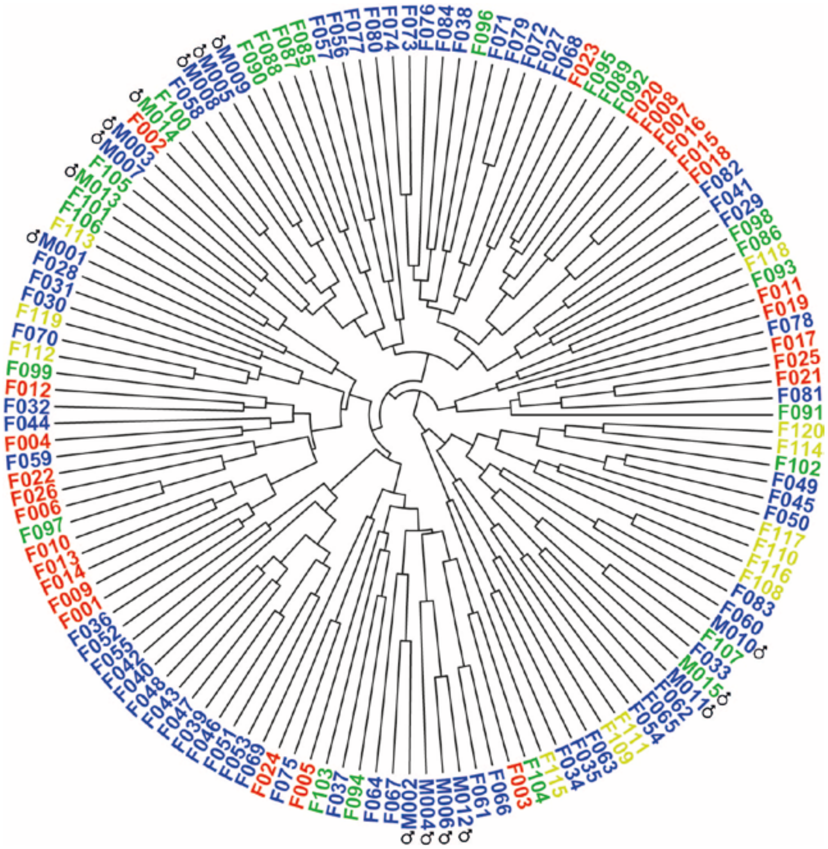

Figure 5. Rogers’ distance-based clustering of 135 parental lines. Lines provided from different companies were marked with different colors

Breeding for improved yield stability is challenging

Hybrid breeding holds the promise to improve the adaptability of varieties to extreme weather conditions because of the improved individual buffering effects (Hallauer et al. 1988). Mühleisen et al. (2014b) reported that winter barley hybrids showed clear advantage on dynamic yield stability performance over lines based on official registration trials. In wheat, group-based estimate of dynamic yield stability performance of experimental hybrids was also better than that of lines (Mühleisen et al. 2014a). In the present thesis, genotype-specific estimates of yield stability parameters obtained from official registration trials in Germany were similar for hybrids and lines (Liu et al. 2017). This surprising finding can be explained by substantial larger investments made in line than in hybrid breeding. The lack of efficient hybridization system for large-scale hybrid wheat production hampers so far the major investments in hybrid breeding. In contrast, market penetrance is much higher for hybrid barley due to the possibility to produce hybrids via a cost-efficient CMS system, leading to higher investment for hybrid barley breeding. Therefore, comparison on yield stability performance between wheat hybrids and lines need to be re-evaluated when efficient hybrid wheat production systems are available.

Yield stability performance is going to be an important criterion for breeding programs to cope with the changing climate. However, estimation of yield stability parameters is much more difficult than grain yield, which impedes the application of yield stability in breeding programs. Precise estimation of yield stability needs intensive phenotyping (**Figure 6**). For breeding programs, field trials were usually conducted in 2-10 locations at different stages (Longin et al. 2014), which could lead to accurate estimation of yield performance with heritability 0.6-0.9. However, the heritability for yield stability parameters is below 0.4 when genotypes are tested at 10 locations. To achieve a heritability of 0.7 for yield stability parameters, 40-50 locations (environments for multi-year trials) are required (Liu et al. 2017), which is challenging for breeding programs.

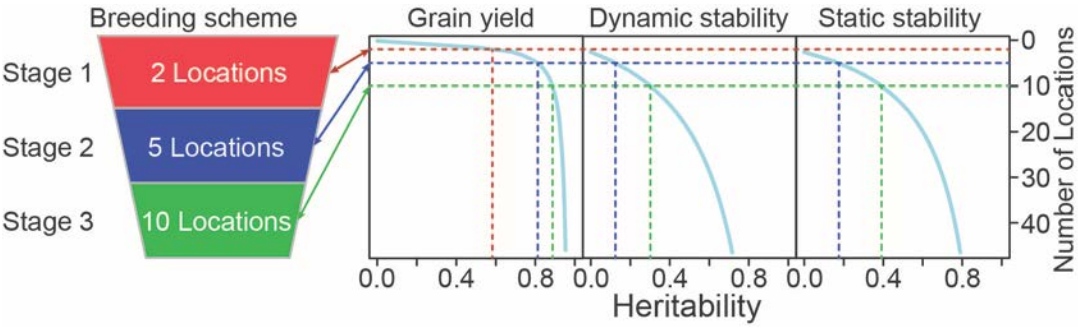

Figure 6. Heritabilities for grain yield, dynamic yield stability, and static yield stability expected in different stages of breeding

Indirect selection is frequently used if the target characters are difficult or costly to measure but genetically linked to secondary characters, which are much easier to assess (Gallais 1984). The potential of indirect selection for yield stability has been investigated for barley (Mühleisen et al. 2014b) and wheat (Liu et al. 2017), which detected associations in some populations. However, such associations were not transferable across populations and were useless for the prediction of yield stability performance in other populations, inferring that indirect selection is not feasible. Alternatively, dissecting the genetic architecture of phenotypic stability have been proposed to improve the efficiency of yield stability estimation; however, studies in wheat (Huang et al. 2016), barley (Kraakman et al. 2004), and rye (Wang et al. 2015) reflect a complex genetic architecture of stability. Liu et al. (2017) suggested an alternative strategy to improve the efficiency of assessing yield stability performance using representative environments selected based on genotype-by-environment interaction effects. This approach significantly improved the prediction ability for yield stability (Liu et al. 2017). However, the critical issue is whether the suggested approach can be successfully implemented based on genotype-by-location interactions. The variances of interactions involving genotypes were mainly dominated by the variance of genotype-by-location-by-year interactions (Liu et al. 2017), which was more than two times larger than the variances of genotype-by-location and genotype-by-year interactions. This observation, however, can be an artifact of the unbalanced genotype-by-location-by-year matrix of the official registration trials. Therefore, further research is required to verify whether the concept of selecting representative locations is a promising strategy or not.

Success of MAS is hampered by the complex genetic architecture for several important agronomic traits

For the experimental hybrid population used in this thesis (**Figure 4B**), the resistance against STB (Mirdita et al. 2015b), FHB (Mirdita et al. 2015b) and quality traits (Liu 2016; Liu et al. 2016) were recorded. The quality traits comprised gluten content, starch content, kernel hardness, protein content, sedimentation volume, test weight, and thousand kernel weights. Genotypic data was generated using a 90k SNP array (Wang et al. 2014). Association mapping was performed to detect QTL correcting for population stratification by modelling a kinship matrix (Yu et al. 2006). This decreased the change of false-positives but validations of the marker-trait associations are still required before using them in applied breeding programs. Marker-trait associations can be validated either by using an independent sample (Melchinger et al. 1998) or by cross validation (Hjorth 1993). Validation using an independent sample is time consuming and impacted from environmental sampling (Utz et al. 2000). Cross-validations are afflicted by relatedness between the in-silico formed test and estimation sets as has been highlighted in the context of association mapping (Jiang et al. 2015). Relatedness between test and estimation sets leads to severely overestimated proportions of explained variation in MAS.

The diversity among the parents of the experimental hybrid population was maximized and the degree of relatedness minimized. We performed a cross-validation approach in this thesis which allows investigating systematically the bias in estimating the prediction accuracies caused by relatedness (**Figure 7**): The estimation sets consisted of ten male (out of 15) and 80 female lines (out of 120) as well as 610 hybrids derived from them. Test sets with three successively decreasing degrees of relatedness to the estimation set were generated. The test sets included only hybrids and shared two parents (T2), one parent (T1), or no parent (T0) with the estimation set. Considering the lowest level of relatedness with the estimation set, the T0 scenario, is the most valuable scenario to validate the potential of MAS.

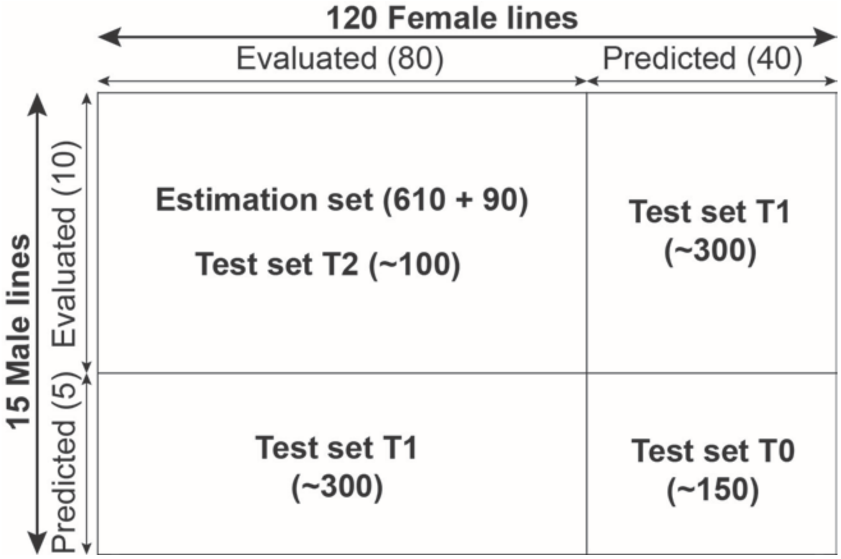

Figure 7. Scheme for allocation of hybrids to estimation set and three test sets

For resistance against FHB and STB, no stable QTL was detected across cross-validation runs in this thesis (Mirdita et al. 2015b). All the quality traits except thousand kernel weight showed absence of stable QTL, leading to extremely low prediction accuracies in T0 scenario (Liu et al. 2016). For thousand kernel weight, five linked SNPs were detected in more than 90 cross validation runs, resulting in higher prediction accuracies in T0 scenario. These marker-trait associations are interesting candidates for MAS. For the remaining traits, complex genetic architectures are expected and GS is a promising alternative.

GS in hybrid wheat breeding

In GS, a large number of markers are considered jointly for performance prediction of a target trait (Heffner et al. 2009). This allows predicting traits with a complex genetic architecture more properly. In the present thesis, the potential of GS was studied for the experimental hybrid population focusing on resistances against FHB and STB, and quality traits. The prediction accuracies of different scenarios were much higher than that observed for MAS (Liu et al. 2016; Mirdita et al. 2015b). Additionally, even the MAS-based prediction accuracy of 1000-kernel weight, for which stable QTL were detected, was much lower than the GS-based prediction accuracy (**Figure 8**), indicating that GS is superior to MAS for the traits investigated in this thesis. Moreover, the findings revealed that prediction accuracy increased substantially with tighter relatedness between the estimation and test sets from the T0 to the T2 scenario.

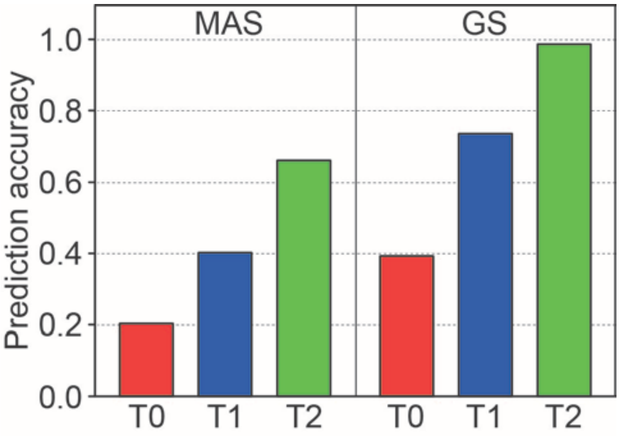

Figure 8. Average prediction accuracies through marker-assisted and genomic selection for 1000-kernel weight

Besides relatedness, the genetic architecture of the trait under consideration can also severely influence the prediction accuracy (Mirdita et al. 2015b). Enhanced relatedness and sufficient reflection of genetic architecture will promote the prediction accuracy. Three further factors, i.e., marker density (Meuwissen 2009), effective population size (Meuwissen 2009), and the used prediction model (Zhao et al. 2014) potentially impact the prediction accuracy. The concept of effective population size was introduced to calibrate for random genetic drift. The effective population size is the size of an ideal population that would undergo the same amount of random genetic drift as the population under study (Lande and Barrowclough 1987). Increasing effective population size of training populations can improve the prediction accuracy (Meuwissen 2009) because of enhanced relatedness between training and test populations. Increasing marker density can also boost prediction accuracy either by enabling a more precise estimation of the relationship among individuals (Habier et al. 2007) or by a better exploitation of the knowledge of the genetic architecture. The optimum marker density is a function of the effective population size (Meuwissen 2009): the larger the effective population size is, the more markers are needed to maximize the prediction accuracies. The prediction accuracy plateaued in the hybrid wheat population at 3,000 markers (Liu et al. 2016), indicating that higher density marker arrays are not needed for the implementation of GS in the underlying population. However, this holds only true for traits with a complex genetic architecture. For traits with major QTL, a high marker density can lead to increased prediction accuracies when choosing a proper prediction model (Zhao et al. 2014). Selection of suitable prediction models strongly depends on the genetic architecture underlying the target traits (Zhao et al. 2015b). The ridge regression BLUP (RR-BLUP) simultaneously estimate effects for all the markers by equally shrinking the marker effects towards zero (Meuwissen et al. 2001; Whittaker et al. 2000). Although the assumption that the effects of all the individual marker have the same variance is unrealistic (Xu 2003), RR-BLUP is superior to MAS and the other GS approaches for traits exhibiting a complex genetic architecture (Whittaker et al. 2000). For traits which are controlled by major QTL, while the incorrect assumption of RR-BLUP will lead to overshrinking of marker effects (Meuwissen et al. 2001; Xu

2003), the Bayesian methods which allows marker effects of differing sizes relax this assumption (Hayes 2007). For traits with major QTL, the weighted-BLUP, which assigns the QTL a fixed effect, could achieve more accurate prediction (Zhao et al. 2014). Thus, an optimized implementation of GS in hybrid wheat breeding requires detailed studies for each trait and population under consideration.

Genomic versus phenotypic selection in hybrid wheat breeding

A crucial criterion for assessing breeding strategies is to compare the annual selection gain (Longin et al. 2007). Longin et al. (2014), in consideration of annual selection gain in hybrid breeding, concluded that a purely GS strategy outperformed the other breeding strategies only if the prediction accuracy exceeds 0.5, otherwise, a combined strategy of GS and phenotypic evaluation is preferred. In this thesis, our results apparently showed that a prediction accuracy of 0.5 is only not reachable in the T0 scenario (Figure 8; Liu et al. 2016; Mirdita et al. 2015b). Consequently, the pure GS strategy is the method of choice for the hybrid performance prediction in T1 and T2 scenarios and combined strategy of GS and phenotypic evaluation achieves maximum annual selection gain in T0 scenario.

However, the above conclusion is based on the comparison of scenarios with low selection intensities. The selection gain depends on the selection intensity and prediction accuracy. Increasing selection intensity is possible to counterbalance the low prediction accuracy via GS, raising the selection gain (Xu et al. 2014). GS could predict the performance of all the possible hybrid combinations among current parental lines. The huge amounts of potential candidates would allow very high selection intensities, achieving higher selection gain than the conventional hybrid breeding approaches.

To sum up, for a specific population, the choice of an optimal breeding strategy is different for these three scenarios. For the T0 scenarios, pure GS is not the method of choice due to the low prediction accuracy within this scenario. However, this holds only true for hybrid breeding programs with low selection intensities. The application of GS allows predicting huge amounts of possible hybrid combinations and the high selection intensity can lead to higher selection gain than the traditional breeding strategy.

Conclusions

Yield stability is of low heritability and precise evaluation of individual based yield stability performance requires intensive phenotyping. Indirect selection and genomic assisted selection is not promising for yield stability. Further research is required to verify the feasibility of the strategy that improves the prediction efficiency for dynamic yield stability by selecting representative locations. For a specific hybrid breeding program, GS is not always the method of choice, although GS outperformed MAS. GS could predict the performance of all the possible hybrid combinations among current parental lines. The huge amounts of potential hybrids would allow high selection intensity, achieving higher selection gain than the conventional hybrid breeding approaches. Prediction accuracy of GS is influenced by the effective population size of the training set, marker density, and prediction models. Well-constructed estimation sets, proper marker density, and a suitable prediction model could maximize the prediction accuracy and thus the economic efficiency of GS.

5. Summary

The consequences of climate change can negatively impact yield of many important crops. Wheat (*Triticum aestivum* L.) as an autogamous species is mainly improved applying line breeding with stagnating yield increase. In contrast, yield increase in hybrid crops is high because of an efficient exploitation of heterosis. Thus, hybrid wheat breeding is a promising approach to boost yield per area and enhance yield stability. The main goals of this thesis were to develop a framework to compare the yield stability of wheat hybrids and lines and to explore the potential of genomics-assisted improvement of wheat hybrids focusing on seven quality traits and resistances to STB and FHB.

A procedure to estimate heritability of yield stability was developed and applied to German official winter wheat registration trials. To achieve a heritability of above 0.7 for yield stability, testing in at least 40 environments is required, which is fulfilled in the case of official registration trials. Interestingly, the few hybrids included in the official variety testing had on average higher grain yield than the group of line varieties but no differences were observed for yield stability. This surprising result can be explained by substantial larger investments made in line than in hybrid breeding. One approach to reduce the required number of environments for assessing precisely yield stability consists in selecting representative environments based on genotype-by-environment interactions. Selecting a posteriori contrasting environments allowed decreasing phenotyping intensity but still maintaining high accuracy to assess yield stability. The huge potential of the developed strategy has to be validated as a next step in an a priori scenario based on genotype-by-location interaction effects.

One challenge in hybrid wheat breeding is to select superior candidates out of millions of hybrid combinations. Marker-assisted selection and genomic selection are two promising alternatives to phenotypic selection in order to identify superior single crosses. The findings of this thesis clearly revealed the superiority of genomic versus marker-assisted selection for seven quality traits and resistances to Septoria tritici blotch and Fusarium head blight. Prediction accuracy is strongly influenced by relatedness between the training and test population which underpinned the need to work with diverse training populations exhibiting a large effective population size. Consequently, it is beneficial to enlarge rather the number of parents than to increase the number of hybrid combinations per parent in the training population. Considering this principle facilitates to successfully implement genomic selection in applied hybrid wheat breeding programs.

6. Zusammenfassung

Die Auswirkungen des Klimawandels können den Ertrag von vielen bedeutenden Kulturarten negativ beeinflussen. Der Weizen wird als Selbstbefruchter hauptsächlich über Linienzüchtung verbessert, allerdings stagnieren die Ertragszuwächse. Im Gegensatz dazu ist der Selektionsgewinn bei Hybridkulturarten hoch was hauptsächlich an der effizienten Nutzung von Heterosis liegt. Daher ist die Hybridweizenzüchtung ein vielversprechender Ansatz, um den Flächenertrag und die Ertragsstabilität zu erhöhen. Die Hauptziele dieser Arbeit waren einen Ansatz zu entwickeln, um die Ertragsstabilität von Hybriden und Linien im Weizen zu vergleichen und das Potenzial der Genomik-basierten Verbesserung von Weizenhybriden für sieben Qualitätsmerkmale und Resistenz gegen Septoria tritici und Ährenfusariosen zu untersuchen.

Ein Ansatz zur Schätzung der Heritabilität der Ertragsstabilität wurde entwickelt und für die Analyse von Daten deutscher Bundessortenversuche verwendet. Um eine Heritabilität von über 0.7 für Ertragsstabilität zu erreichen, sind Versuche in mindestens 40 Umwelten notwendig. Dies ist der Fall für Bundessortenversuche. Interessanterweise waren die wenigen geprüften Hybriden im Mittel ertragsreicher als die Linien allerdings zeigten sie keinen Unterschied in der Ertragsstabilität. Dieses überraschende Ergebniss kann über substantiell höhere Investitionen in die Linien- im Vergleich zur Hybridzüchtung erklärt werden. Ein Ansatz um die Anzahl an Umwelten für die präzise Erfassung der Ertragsstabilität zu senken, besteht in der Auswahl von repräsentativen Umwelten basierend auf den Genotyp mal Umweltinteraktionseffekten. Eine a posteriori Selektion ermöglichte, die Anzahl der Umwelten zu reduzieren ohne dabei die Genauigkeit der Schätzung der Ertragsstabilität zu verringern. Das große Potenzial der entwickelten Strategie muss nun im Folgenden in einem a priori Szenario basierend auf Genotyp mal Ortsinteraktionseffekten validiert werden.

Eine der großen Herausforderungen der Hybridweizenzüchtung ist die Selektion von überlegenen Kandidaten aus den Millionen möglichen Hybridkombinationen. Marker-gestützte und genomische Selektion sind zwei vielversprechende Alternativen zur phänotypischen Selektion, um überlegene Hybriden zu identifizieren. Die Ergebnisse dieser Arbeit zeigen klar die Überlegenheit der genomischen im Vergleich zur Marker-gestützten Selektion für sieben Qualitätsmerkmale und Resistenzen gegen *Septoria tritici* und Ährenfusariosen. Die Vorhersagegenauigkeit wird stark von der Verwandtschaft zwischen Trainings- und Testpopulation beeinflusst, was die Notwendigkeit mit diversen Trainingspopulationen mit hoher effektiver Populationsgröße zu arbeiten verdeutlicht. Folglich ist es vorteilhaft, die Anzahl der Eltern anstatt die Anzahl der Hybridkombinationen pro Elter in der Trainingspopulation zu erhöhen. Die Berücksichtigung dieses Prinzips erlaubt eine erfolgreiche Implementierung der genomischen Selektion in die Hybridweizenzüchtung.

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8. Abbreviations

CHA	Chemical hybridizing agent
CMS	Cytoplasmic male sterility
FHB	Fusarium head blight
GCA	General combining ability
GS	Genomic selection
GWAS	Genome-wide association study
MAS	Marker-assisted selection
MP	Mid-parent
QTL	Quantitative trait locus/loci
RR-BLUP	Ridge regression best linear unbiased prediction
STB	Septoria tritici blotch
W-BLUP	Weighted best linear unbiased prediction

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Ich erkläre an Eides statt, dass ich die Arbeit selbstständig und ohne fremde Hilfe verfasst, keine anderen als die von mir angegebenen Quellen und Hilfsmittel benutzt und die den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen als solche kenntlich gemacht habe.

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