

Minireview Article

Prediction of Heterosis in Crop Plants – Status and Prospects

ABSTRACT

Heterosis has been commercially exploited in many crops; however, its genetic and molecular basis is still not clear. The availability of advanced genomic tools has encouraged several research groups to dissect heterosis into genetic components. Prediction of heterosis using molecular markers is the first step towards this direction, as it may lead to the identification of markers and genomic regions associated with heterosis. Practically, it increases the efficiency of hybrid breeding by marker-assisted selection of superior parental combinations without large-scale field evaluation. Extensive studies in important crops like rice, wheat and maize have identified the genes / genomic regions associated with heterosis and also demonstrated the potential of molecular prediction. Recent trends in whole transcriptome and metabolome analyses will help in the identification of genes or metabolic networks involved in the expression of heterosis. Various genomic tools such as heterotic loci, molecular markers associated with heterotic gene blocks, ESTs and heterosis-related gene databases provide better opportunities for understanding the molecular basis of heterosis and to develop reliable methodologies for a realistic prediction of heterosis. This review provides critical analysis of the prediction of heterosis in crop plants and its implications in hybrid development.

Keywords: Heterosis; molecular markers; genetic distance; prediction methods; gene expression

1. INTRODUCTION

Development of hybrids through the exploitation of heterosis is considered as one of the greatest breakthroughs in plant breeding, as evident from the dramatic increases in the productivity of many crops. In crops like maize, sugarbeet, sunflower, sorghum, pearl millet and many vegetable crops, hybrids are grown predominantly, whereas in many others, like rice, cotton, safflower and rapeseed the area under hybrids is rapidly increasing. Even though the genetic and molecular basis of heterosis is still unclear, plant breeders continue to exploit heterosis extensively to develop superior hybrids. The development of molecular markers and saturated linkage maps has offered useful tools to dissect the complex trait of yield and other agriculturally important traits into genetic components through quantitative trait loci (QTL) analysis, which may lead to a better understanding of the genetic basis of heterosis. Some of the recent research is also focused on the identification of heterotic loci [1, 2, 3] and the molecular markers associated with them thereby helping in understanding the phenomenon of heterosis at the molecular level. In addition, complementary approaches involving genomic, transcriptomic, proteomic and metabolomic data coupled with mathematical modeling [4, 5, 6, 7] have resulted in a better prediction of heterosis in comparison to a single approach. The growing interest for the prediction of heterosis in different crops necessitates the prediction of heterosis in crop plants using phenotypic as well as molecular data including DNA markers (SSR and SNPs), gene expression, profiling of proteins and metabolites. The progress made during the last two decades in improving heterosis prediction in plants using various molecular tools has been discussed critically in this review.

2. PREDICTION OF HETEROSIS

Heterosis refers to the superiority of F_1 hybrids with respect to biomass, size, yield, rate of development, fertility, biotic and abiotic stress tolerance compared to the average of their parental inbreds [8, 9]. Breeders have to evaluate a large number of parental lines for their combining ability, make thousands of test crosses and evaluate the F_1 hybrids for yield heterosis to identify the best hybrid. This consumes a lot of resources and time. Moreover, the field trials can accommodate only a limited number of crosses in all possible combinations between the parental lines, and the results are subjective. Therefore, hybrid breeders have always been interested in the selection of potential lines among the available parental lines which are expected to give heterotic hybrids by-passing the field evaluation of a large number of crosses involving these parental lines. Over the years, several methods were employed to predict heterosis, such as, *per se* performance of parental lines, mitochondrial complementation, combining ability and genetic diversity estimated from geographical origin, coefficient of parentage, multivariate analysis of morphological traits and isozyme and molecular marker analysis. Among these methods, mitochondrial complementation based heterosis prediction is unpopular since the results were not reproducible. Hence, this method will not be discussed further in this review. Apart from these methods, gene expression is being used in recent studies to predict heterosis.

2.1 Phenotypic Data-based Prediction of Heterosis

Heterosis prediction can be done through *per se* performance of parental lines, combining ability and genetic diversity studies using the phenotypic data collected from field evaluation of genotypes. Several studies in different crops reported contrasting conclusions regarding the effectiveness of *per se* performance in the prediction of heterosis. Studies in maize [10] and sugarcane [11] concluded that there was no association between *per se* performance of parental lines and heterosis in F_1 hybrids. Selection of potential parents based on *per se* performance was found to be effective in Triticale for traits other than grain yield [12], while in tropical maize the performance of hybrid progenies under excessive moisture stress can be predicted, to some extent, based on *per se* performance of their inbred parents that were selected and improved for excessive moisture stress [13]. Therefore, it can be concluded that heterosis prediction based on *per se* performance of parents may not be a reliable indicator of heterosis.

Identification of superior parental lines for developing heterotic hybrids was generally done by employing combining ability tests such as top-cross test, poly-cross test, single cross test, diallel mating, and line $\times$ tester analysis, though with variable levels of success [14]. In general, selection of parental lines with high general combining ability (GCA) effects resulted in the development of heterotic hybrids in any crop. However, heterotic combinations could also be derived from parents exhibiting low GCA effects as noticed in rice [15] and such combinations could not be derived from parents with high GCA [16]. Studies in crops like maize [17], wheat [18], Ethiopian mustard [19] and rapeseed [20] have shown moderate to strong correlation between combining ability and *per se* performance as well as mid-parent heterosis, but in varying degrees. It is important to note that the strong relationship between the mean performance and GCA of inbred lines may be due to the presence of additive genetic variance. SCA is related to heterosis but the association is more tricky than assumed. However, the non-additive genetic variance or specific combining ability (SCA) is ignored here, which will drastically reduce this correlation. Therefore, SCA has to be given due **considered** since it has a direct impact on heterosis.

The extent of genetic diversity between the two parents has been proposed as a possible indicator for the prediction of heterosis [9, 21]. However, heterosis and genetic diversity

between parents rarely exhibit a strong correlation [22, 23, 24]. More reports have been published in maize [25] and rice [21, 26, 27], but the extent of correlation varied widely from one trait to another and from one data set to another. In Ethiopian mustard, Teklewold and Becker [28] reported that it was possible to predict the heterosis and parental combining ability to some extent based on genetic distance calculated over phenotypic traits. However, in sorghum, a perfect correspondence between heterosis and genetic diversity between parental lines was lacking (Rani and Rao 2009). Due to lack of consistency in the prediction of heterosis based on genetic diversity and combining ability among parental lines through field evaluation, there is an immense need for the prediction of heterosis based on the molecular marker polymorphism from a large pool of parental lines without field evaluation. The present review discusses mainly on the prediction of heterosis based on molecular marker data and gene expression data, such as transcript abundance and expression levels/patterns that are becoming popular in the prediction of heterosis.

2.2 Molecular Marker-based Prediction of Heterosis

Genetic divergence of parental lines is thought to be related to heterosis or hybrid vigor of the hybrid as discussed earlier. Thus, biochemical and molecular marker-assayed genetic variation of the parental lines may potentially be useful for predicting heterosis. Prior to molecular markers, isozymes were the commonly used biochemical markers for the prediction of heterosis. Many of the studies in maize used only fewer isozyme loci as well as limited parental lines. As a result, low and non-significant correlations were reported in these studies between isozymes diversity and specific combining ability. Even in a study involving 100 maize hybrids derived from 37 parental lines at 11 isozyme loci, an R² value of only 0.36 was reported [29]. Furthermore, in a study in rice, no association was observed between isozyme diversity and grain yield of hybrid using six isozyme loci in 75 F₁ hybrids [30]. Distances computed from isozyme data were in some cases significantly correlated to heterosis but their utility in the prediction of heterosis was limited primarily to lines with similar pedigrees [31]. Isozymes were considered to be unpopular for heterosis predictions since they could sample only a limited number of loci contributing to the hybrid response and it is unlikely that these loci will have a direct effect on the phenotypic expression of the targeted trait [32].

One of the important challenges that have encouraged research in employing molecular markers and genomics in heterosis breeding relates to the understanding of genetic and molecular bases of heterosis and prediction of heterosis. The use of molecular markers led heterosis prediction into a new phase since it appeared in 1980s, but the conclusions were not consistent with each other. High positive correlation of yield heterosis with genetic distance based on RAPD and SSR markers was reported for *indica* x *indica* and *japonica* x *japonica* crosses but not for *indica* x *japonica* crosses [33]. Significant and effective correlations between genetic distance and heterosis were reported in rice [26, 34], maize [25], wheat [35], sunflower [36] and rapeseed [37]. On the other hand, weak or non-significant correlations have also been reported between genetic distance and heterosis in some studies. Table 1 summarizes the studies conducted on the prediction of heterosis using molecular markers in different crops and their conclusions.

With the prominence and popularity of single locus markers, especially microsatellite markers, several efforts were made in rice in assessing the utility of SSR markers for heterosis prediction based on the relationship between molecular diversity of parental lines and heterosis of the resulting hybrid [42, 43, 44, 72]. Consistency in the prediction was lacking in these studies, and this may be because prediction of heterosis was based on genetic diversity of anonymous molecular markers, which may not be associated with functional regions of the genome. Therefore, prediction based on functional markers,

137 especially the markers associated with genes controlling heterosis for yield traits, might be
 138 more powerful than that based on anonymous markers. Markers used for prediction of
 139 heterosis should be differentiated into positive markers, since every marker is not linked to a
 140 quantitative trait locus (QTL) and therefore, with heterosis [27]. It was also suggested to use
 141 QTL-linked markers, thus distinguishing between general and specific heterozygosity. An
 142 attempt was made in rice to associate morphological traits, pedigree records and SSR
 143 polymorphism with heterosis [42]. While no significant correlation was observed for
 144 morphological traits and pedigree records, a low correlation value was noticed between SSR
 145 polymorphism and heterosis. They also reported that molecular markers would be useful for
 146 predicting hybrid performance only when a significant portion (>50%) of the selected
 147 markers is linked to QTL. In a study  rice, genomic and EST-SSR marker polymorphism
 148 was compared for its correlation with heterosis and concluded that the latter exhibited a
 149 significant positive correlation with heterosis resulting in the identification of 10 informative
 150 EST-SSR markers having the potential for the prediction of heterosis [45]. Once such
 151 informative markers are identified, they should be tested in different populations of parental
 152 lines varying in their genetic background to ascertain their consistency in the prediction of
 153 heterosis. Moreover, it is also important to analyze the expression of these genes in hybrids
 154 and their parents to understand their role in heterotic expression.

155 Molecular markers are widely used in QTL mapping of quantitative traits [73, 74, 75] and
 156 exploration of genetic diversity, with the latter often employed in the prediction of heterosis
 157 [27, 41, 76]. Methods using the genetic distance between the parental lines estimated using
 158 random/anonymous molecular markers failed to predict reliably the hybrid performance and
 159 hence prediction methods using markers linked to QTL were successfully developed. The
 160 advantage of using such markers is that it can reveal the locus and/or locus pair that could
 161 be targeted for improvement in further breeding programs by manipulating the related QTL
 162 [77]. Unfortunately, studies on the prediction of heterosis based on analysis of polymorphism
 163 of yield related QTL are limited. Neither heterozygosities nor QTL for yield traits were found
 164 to be suitable to predict hybrid performance and heterosis in *Brassica napus* [67]. On the
 165 contrary, a study in rice indicated that the QTL identified for 1000-grain weight showed a
 166 high contribution to heterosis. The heterosis over mid-parents of QTL could be predicted
 167 based on QTL effects [78]. A total of 13 heterotic loci in maize [1], genome regions harboring
 168 numerous heterosis-related QTL in oilseed rape [3] and 10 genomic positions involved in
 169 biomass heterosis during early development in *Arabidopsis* were identified [2]. Very recently,
 170 Ben-Israel et al. [79] identified three heterotic trait loci with synergistic intra-locus effects on
 171 grain yield heterosis in sorghum, which accounts for 19.0% of the heterotic variation,
 172 including a significant epistasis between two of them. Also, a significant 21% increase in
 173 grain yield was observed for one of these loci (hDPW4.1) in a consecutive F₂ population.
 174 Such studies  help to identify the QTL/genomic regions associated with heterosis and
 175 markers associated with them may help in a better prediction of heterosis. If successful,
 176 such prediction methods may lead to the selection of the limited number of parental
 177 combinations for synthesizing experimental hybrids for field evaluation for the identification
 178 of highly heterotic hybrids, thus increasing the efficiency of hybrid development.

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Table 1 Heterosis prediction studies in different crops using molecular markers

Crop Species	Marker type	Plant material	Conclusions and References
Rice	RFLP	11 elite lines in a diallel set involving <i>indica</i> and <i>japonica</i>	Complex relationship was observed between marker heterozygosity and hybrid performance [38].
	RAPD, ISSR, RFLP and STMS	Two CMS lines, four restorers and 28 hybrids	Molecular markers may not always be useful for selection of parents [39].
	SSR and RAPD	13 'Tongil'-type rice cultivars and 78 hybrids	DNA marker-based GD may not be useful for heterosis prediction [40].
	AFLP	Eight CMS lines, 10 restorers and 80 hybrids	Heterosis was related to GD between the parents, with a few loci contributing to it [41].
	Pedigree record, quantitative traits and SSR	37 maintainers, 43 restorers and 34 hybrids	Prediction is difficult through SSR and pedigree-based diversity of complex traits [42].
	RAPD and SSR	41 hybrids from a half diallel with 10 <i>japonica</i> cultivars	Proposed the role of 'key' DNA markers in the prediction of heterosis [43].
	SSR	13 CMS lines, 19 restorers and 151 hybrids	Prediction of heterosis based on effect-increasing loci was more effective [44].
	SSR and EST-SSR	Nine CMS lines, 32 restorers and 20 hybrids	Prediction of heterosis is better using EST-SSRs [45].
Maize	RAPD	18 inbred lines	DNA marker are useful in aiding the choice of superior crosses to be made [46].
	RFLP	Eight and 10 S ₃ selected inbred lines in partial diallel	RFLP-based GDs are not useful for the prediction of heterosis [47].
	AFLP	53 inter-heterotic hybrids of a 13 × 13 half-diallel	Some QTL of grain yield were located in the vicinity of loci having quantitative effects on grain yield [48].
	Morphological data and RAPD	28 open pollinated varieties in a diallel scheme and 378 hybrids	Low and positive correlation was observed between RAPD-based GD and SCA for yield [49].
	RAPD	13 inbred lines and 78 hybrids	RAPDs are not suitable for the prediction of yield performance of hybrids [50].
	AFLP and SSR	18 S ₃ inbred lines in a partial diallel mating design	Single cross performance can be predicted through AFLP-based GD [51].
	SSR	15 elite inbred lines and 105	Prediction of yield heterosis using SSR markers is difficult [52].

	AFLP	hybrids 52 maize elite inbred lines and 270 hybrids	Prediction efficiency ranged from 0.46 to 0.86 for grain yield and from 0.59 to 0.96 for grain dry matter content [53].
	AFLP	52 elite inbred lines and 270 hybrids	Prediction of heterosis improved by variable haplotype block length than with AFLP markers [54].
	AFLP	21 inbreds and 225 hybrids	Integration of molecular and phenotypic data will lead to better prediction of heterosis [55].
	AFLP	26 inbred lines were crossed with six testers	Significantly positive correlations with low magnitude between GDs and mid-parent heterosis can be of predictive value [56].
	AFLP	400 hybrids from nine factorial crosses and 79 inbred parents	Even without testcross data of parents, the hybrid performance was predicted efficiently by molecular markers [57].
Wheat	RFLP and RAPD	Eight-parent diallel cross and top cross (4 males × 25 females)	A weak correlation was observed between parental diversity and hybrid performance [58].
	RAPD	10 CMS lines, 10 restorers and 41 hybrids	No significant correlation was observed between RAPD marker-based GD with heterosis [59].
	RAPD	18 parental lines and 76 F ₂ hybrids	GDs between parents can be a potential predictor of hybrid performance for selected traits [60].
Sorghum	RFLP	162 hybrids derived from 70 inbred lines	Very weak association of GD with yield is of no value for identifying superior hybrids [61].
	SSR	210 hybrids from 37 parental lines	A significant, positive and moderate correlation between coefficient of marker polymorphism of parental lines with grain yield heterosis of their respective hybrids indicated the potential of molecular marker-assisted prediction of heterosis [62].
	AFLP, SSR and SRAP	90 cross combinations five sterile lines and 18 Sudan grass lines.	An average correlation was observed between molecular marker value and grain yield heterosis ($r = 0.65$), which will help breeders to exploit the markers associated with yield QTL for a reliable prediction of heterosis [63].
Triticale	SSR and AFLP	206 F ₁ crosses and 61	Low correlations between GD and SCA hampered the

		parental lines	prediction of SCA from molecular data [64].
<i>Brassica napus</i>	SRAP	10 maintainer lines and 12 restorers	Correlation coefficient between GD and yield (0.64) indicated a moderately strong relationship [65].
Oilseed rape	Morphology, isozymes, proteins and RAPD	Six male-sterile lines, five restorers and 30 hybrids	GD based on significant and favorable markers significantly correlated with plant height, seeds per silique and seed yield [66].
Rapeseed	AFLP and SSR	Three double low (erucic acid and glucosinolates) self-incompatible lines, 22 varieties and 66 hybrids	Neither heterozygosities nor QTLs for yield traits were suitable for predicting heterosis [67].
Faba Bean	AFLP	18 inbreds, 62 hybrids and their F ₂ progenies	AFLP-based genetic similarities are not useful to predict heterosis [68].
Pepper	Morphology and AFLP	Seven parents and 21 hybrids	Correlations of AFLP-based GDs with mid- and high-parent heterosis were non-significant and proved to be of no predictive value [69].
Cotton	RAPD and SSR	Three CMS lines, 10 restorers and 22 hybrids	The relationship between SSR marker heterozygosity and hybrid performance can be used to predict fibre length during inter-specific hybrid cotton breeding [70].
Chickpea	RAPD and SSR	Eight genotypes in diallel set	Two heterotic groups could be identified on the basis of the general marker heterozygosity [71].

Abbreviations: RFLP, restriction fragment length polymorphism; RAPD, randomly amplified polymorphic DNA; ISSR, inter-simple sequence repeats; AFLP, amplified fragment length polymorphism; SSR, simple sequence repeats; STMS, sequence tagged microsatellite sites; SRAP, sequence related amplified polymorphism; EST, expressed sequence tag; GD, genetic distance; QTL, quantitative trait loci; SCA, specific combining ability

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3. METHODS FOR IMPROVING THE PREDICTION OF HETEROSIS

Even though molecular marker systems such as restriction fragment length polymorphism (RFLP), randomly amplified polymorphic DNA (RAPD), inter-simple sequence repeats (SSR) and amplified fragment length polymorphism (AFLP) were used earlier for the prediction of heterosis, the studies ended up with limited success. This may be because each marker system differs in their ability in predicting heterosis. The RFLP data was found to be promising for the prediction of hybrid performance for crosses between lines from the same heterotic group, practically zero for crosses between lines from divergent heterotic groups, and medium for mixtures of both [80, 81]. The correlation between RAPD-based genetic distances and hybrid performance were very low to predict heterosis [39]. A significant improvement in the correlations between genetic distance and hybrid performance was observed in maize by using AFLP markers as compared to RFLP markers due to the analysis of a large number of pre-selected markers linked to quantitative trait loci [82]. Significantly higher correlations between the coefficient of parental polymorphism and heterosis were obtained using EST-SSR markers in rice [45] in comparison to genomic SSR markers.

Heterosis is presumed to be due to heterozygosity and hence the selection of the appropriate type of marker is very important for assessing the genetic diversity among the parents. Codominant and single locus markers such as SSRs and SNPs are advantageous, since they could estimate the heterozygosity based on the parental alleles. This will also help in the identification of specific alleles associated with heterosis of various traits that can be employed in the improvement of inbred parents. Moreover, with the sequencing of crop genomes, these markers can be easily located in the physical map. In contrast, the dominant markers are not informative, since they possess information on the allele of only one parent at a particular locus. Such lack of complete allelic information will be a great setback for the parental line improvement aimed at enriching of superior alleles.

Several efforts were made to improve the power of heterosis prediction. A study based on computer simulations concluded that at least 30-50% of the molecular markers should be linked to QTL while not more than 20-30% of the molecular markers should be randomly dispersed [83]. Later, TM-BLUP (trait marker-best linear unbiased prediction) was developed, which takes into account the molecular marker data together with the trait data for the prediction of hybrid performance. This approach slightly improved the quality of the prediction [84, 85]. A linear regression model, namely TCSM (total sum of selected markers) with a promising predictive power was developed for the prediction of hybrid performance, which calculates genotypic value of hybrids by considering joint effect of genetic factors [48]. This approach was later improved by involving multiple regression as well as haplo-block organization of markers [53, 54, 57]. With the availability of the heterosis related genes of rice, maize and wheat in the public database (Heterosis related genes database, <http://hrgd.big.ac.cn/index.html>) [86], PCR-based molecular markers can be developed and used for the prediction of heterosis in other closely related crop species. Development of SSR or INDEL markers from heterosis related genes is not explored until now and the use of such molecular markers associated with heterosis will help in the reliable prediction of heterosis in comparison to prediction using random/anonymous markers.

4. EMERGING CONCEPTS IN MARKER-BASED PREDICTION OF HETEROSIS

The concept of heterosis prediction using molecular markers has been refined for more than two decades since it appeared in 1980s. Initial predictions with isozymes did not gain importance due to the availability of a limited number of loci and inconsistent results. Later, DNA markers such as RFLPs, RAPDs and ISSRs were predominantly used during the

1990s with very limited success since the correlation between genetic diversity based on these markers with heterosis was very low to predict heterosis. The popularity of SSR markers during the late 1990s resulted in several studies in different crop species towards the prediction of heterosis with the help of SSR-based genetic distance. To start with, anonymous markers (genomic SSR markers) were used, which led to inconsistent results. Then, the focus was shifted to the selection of specific markers based on their effects with heterosis or QTL information instead of using random markers.

A series of studies in rice for the past two decades resulted in the development of the concept of heterosis prediction. The concept has evolved from anonymous or random markers to specific or informative markers. Specific heterozygosity of positive markers (markers with significant effects on the target traits) showed a high correlation with heterosis for grain yield in rice [21]. The importance of significant correlations of specific heterozygosity based on the small number of positive markers (markers associated with heterotic yield response) with hybrid performance than those with general heterozygosity in the prediction of heterosis was also reported [27]. Favorable and unfavorable SSR alleles significantly affecting yield heterosis were identified with a possible use in hybrid rice breeding [26]. Another study revealed that the presence of loci with positive or negative effects, and their counteraction if the total loci were used to heterosis prediction [76]. Markers associated with hybrid vigor and hybrid weakness were identified in rice [43], and they proposed a new concept of 'key DNA markers' for the prediction of heterosis. In line with this, the concept of 'effect-increasing' loci was proposed recently for the prediction of hybrid performances in *indica* rice [44]. Comparative analysis of genomic and EST-SSR markers in rice revealed that the latter exhibited a significant positive correlation with heterosis. A set of informative markers was identified for the prediction of heterosis by a careful and critical analysis of EST-SSR markers [45]. The concept of heterosis is summarized in Fig. 1.

In sorghum, recent studies have highlighted the potential of molecular marker-assisted prediction of heterosis. Correlation of molecular marker polymorphism between parental lines with the grain yield heterosis of their respective hybrids resulted in the identification of a set of 30 SSR markers exhibiting the potential for the prediction of heterosis [62]. Using yield-related QTL, a moderate correlation ($r=0.65$) was observed between the marker value of these loci and yield heterosis, which will help the molecular breeders to exploit such loci for a reliable and accurate prediction of heterosis [63]. In all the above discussed reports, it is very clear that molecular marker-based prediction of heterosis should not involve the total markers, but, selective or informative markers, which will increase the reliability and accuracy of prediction.

5. PREDICTION OF HETEROSIS USING TRANSCRIPTOME AND METABOLOME DATA

Besides molecular marker data, the transcriptomic and metabolomic data also have the potential for the prediction of heterosis. This can be attributed to the fact that heterosis is a genome-wide phenomenon involving a network of genes and proteins leading to changes in the plant metabolism. Rapid advances in this area provide new avenues for the expression-based prediction of heterosis. Several projects investigating the phenomenon of heterosis in different crop species have contributed to the identification and characterization of differentially expressed genes (DEGs) related to heterosis. Among the various techniques applied to identify genes possibly associated with heterosis, differential display analysis, cDNA-AFLP and microarrays have been more popularly used. Analysis of the differential expression of genes at different developmental stages of hybrids and their parental lines have proven to be a useful methodology to identify the genes associated with heterosis.

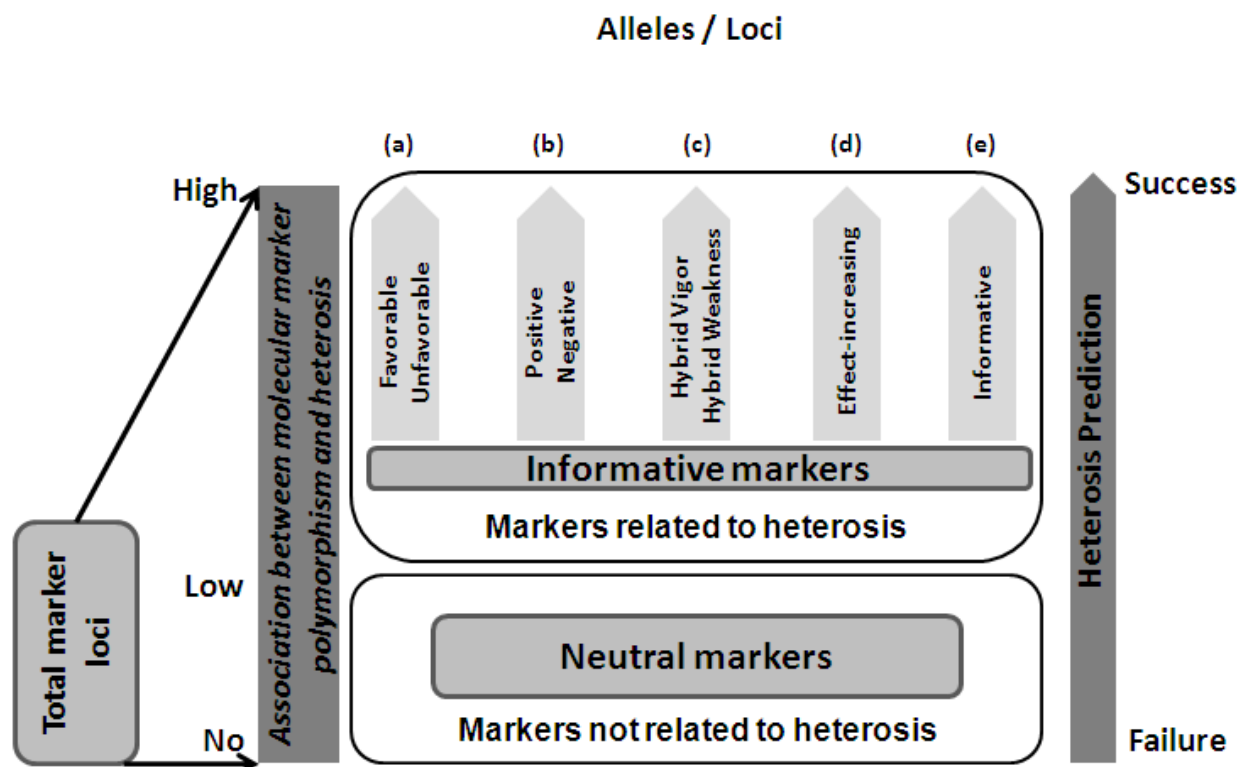


Fig. 1 Concept of heterosis prediction in crop plants. The concept can be summarized based on few important studies that led to the identification of specific marker loci / alleles for the prediction of heterosis viz., (a) 'favorable and unfavorable' SSR alleles [26], (b) loci with 'positive or negative' effects [76], (c) 'hybrid vigor and hybrid weakness' alleles [43], (d) 'effect-increasing' loci [44], (e) 'informative' markers [45].

Earlier studies have indeed indicated that the differential gene expression patterns were correlated with heterosis [87, 88]. The levels of expression of some differentially expressed genes in the parents exhibited highly significant correlations with heterosis and hybrid performance for grain yield and also with grain dry matter content [89]. Such a strong correlation provided the evidence on the prediction potential of genes and their expression levels. Recent studies on the transcriptome-based prediction of heterosis showed promising results. Based on a study in maize, it was concluded that the prediction of hybrid performance was more precise with transcriptome-based distances using selected markers than earlier prediction models involving DNA markers or the estimates of general combining ability [90]. A novel method of predicting heterosis involving a combination of transcriptomic technology and mathematical modeling was developed [91] that could identify a sub-group of genes based on the correlation of their transcript abundance with the magnitude of heterosis in hybrids using linear regression algorithms. Moreover, the allelic patterns of inbreds can be used as potential markers for the prediction of heterosis in hybrids developed from these lines. This approach successfully demonstrated in *Arabidopsis thaliana* and maize can also be employed in other crops reliably predict hybrid vigor for important traits, including yield. In addition, development of molecular markers for heterosis using the transcriptome data was found to be promising even with a limited number of hybrids as well performance data [6]. However, the use of such approach needs further development and evaluation before being applied in hybrid breeding programs.

The applicability of morphological characters, isozymes, proteins, expression profiles, SNP markers, and metabolites in different combinations for prediction of heterosis was investigated by various research groups. Genetic markers were employed in combination with morphological characters, isozymes, and proteins for the same purpose in oilseed rape [66]. In *Arabidopsis thaliana*, it was demonstrated that parental genetic markers in combination with metabolic markers, identified via feature selection and regression methods, significantly improves the prediction of biomass heterosis in the hybrid [4]. Though genetic markers provide very little information, especially in the case of genes with minor effect, more integrated markers such as the levels of plant metabolites, will contribute a decisive part of information, since they represent the combined effect of many genes. A proof of concept of a new complementary approach for the prediction of hybrid biomass in *Arabidopsis thaliana* was presented that involves metabolite profiles in addition to SNP markers and feature selection procedure instead of the whole set of SNPs and metabolites [5]. Recently, whole genome prediction (WGP) was suggested to be a powerful complementary approach in hybrid breeding for highly polygenic traits as revealed prediction accuracies in the range of 0.72 - 0.81 for SNPs and 0.60 - 0.80 for metabolites thereby a reliable screening of a large pool of diverse inbred lines is possible to identify potential parental lines for the development of superior hybrids [7].

Gene expression based approaches are expensive and demands sophisticated infrastructure and expertise. Hence, they may not be suitable for the routine screening of the large number of parental lines for the identification of superior parental combinations. So, there is an immense need for the development of easy, cheap, rapid and routinely usable assays that will help those involved in hybrid development to predict heterosis in different crops. In this direction, a better and pragmatic approach would be the use of PCR-based markers targeting the sequence polymorphism responsible for the differential gene expression in the hybrid as compared to the parents for the prediction of heterosis.

6. FUTURE PROSPECTS

According to Springer and Stuper [92], "heterosis does not simply result from the overall genetic diversity within a hybrid, but is likely a reflection of diversity at specific, important genes that contribute to a particular trait". Therefore, a reliable and accurate prediction of heterosis will depend on exploitation of complex metabolic networks involving several genes or genomic regions. Recent studies discussed in this review highlighted a careful selection of molecular markers is important for a better prediction of heterosis and no single category such as anonymous or QTL linked markers could serve the purpose, however, a major proportion of the markers should be linked to QTLs for the trait of interest. Therefore, it would be better to select a judicious mix of anonymous markers, EST/gene-based markers and QTL-associated markers for heterosis prediction. The genomic selection approach to predict general as well as specific combining ability effects have also been evaluated in maize [93]. Advances in transcriptomics, proteomics and metabolomics have helped to focus research towards the identification of the complete network of genes responsible for different pathways, including those of transcription factors. The popular approach involving whole transcriptome analysis in a hybrid in relation to its parents helps in the identification of genes associated with heterosis. Hence, the future prediction strategies should integrate the valuable information in these data along with molecular marker information to develop a rapid, cheap, efficient and easy-to-use assay to achieve a realistic prediction of heterosis. The current focus in many crops should be on the identification of sequence polymorphisms in the regulatory regions of genes involved in heterotic expression will help to develop a practically viable molecular marker-based approach that targets such a polymorphism responsible for the heterotic expression of different traits. Once genes/genomic regions/QTL associated with heterosis are identified as a consequence of current heterosis projects in

important crops, genetic transformation and marker-assisted introgression can be employed for the enrichment of heterotic genes/alleles in the parental lines so that the resultant hybrid will exhibit high heterosis.

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