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Article · August 2016

DOI: 10.1007/978-3-319-31703-8_3

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QTL Analysis in Plants: Ancient and Modern Perspectives

Muhammad Jamil, Aamir Ali, Khalid Farooq Akbar, Abdul Aziz Napar, Alvina Gul, and A. Mujeeb-Kazi

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M. Jamil (✉) • A. Ali
Department of Botany, University of Sargodha, Sargodha, Pakistan
e-mail: jshahid80@yahoo.com

K.F. Akbar
Department of Botany, Govt. Post-Graduate College, Sahiwal, Pakistan

A.A. Napar
Department of Plant Sciences, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan

A. Gul (✉)
Atta-ur-Rehman School of Applied Biosciences (ASAB), National University of Science and Technology (NUST), Islamabad, Pakistan
e-mail: alvina_gul@yahoo.com

A. Mujeeb-Kazi
Wheat Wide Crosses Program, National Agricultural Research Center (NARC), Islamabad, Pakistan

K.R. Hakeem et al. (eds.), *Plant Omics: Trends and Applications*,
DOI 10.1007/978-3-319-31703-8_3

Abstract Quantitative traits exhibit continuous variation, indicating their control through multiple genes. Segregating populations are used to mine out associations between phenotypic and genotypic variations. Phenotyping performed for a specific trait and its variation in the population is justified with genotypic variation obtained through genetic markers application. A snapshot of genotypic variation is strictly dependent on the number and density of the markers applied. Parental and marker information is required to correlate genetic and phenotypic data for quantitative trait loci (QTL) analysis. For many years (now becoming obsolete), it has been of core importance to identify QTL with such methodology. Failure had to be faced by the researcher because the DNA region identified for phenotypic variation was much wider, and needed to be narrowed down by further dense marker application in that area to obtain required and accurate results. Nowadays the focus is on high-throughput technologies to obtain genome-wide resolution: high-throughput sequencing (HTS) is one of them. A comprehensive map of genomic variations can be produced with resequencing or reference genome sequences. Along with expression profiling, new molecular markers can be searched out with QTL analysis. Genomic-assisted breeding by studying the evolutionary variations in crops has many applied aspects as well. As compared to the conventional biparental population, presently the focus is on raising multiparent advanced generation inter-cross (MAGIC) populations to explore the genetic basis of quantitative traits. Probabilities of alleles of interest across the whole genome are calculated through the Hidden Markov Model (HMM). Different software packages (such as R-package, Qgene) are used for the estimates. Such whole-genome approaches in QTL analysis are a powerful and recently used technique. In this chapter, all these recent and modified modern techniques are reviewed with the most recent upcoming details. Traditional and modern QTL analyses have clearly been differentiated on applicable grounds.

Keywords QTL • Genotyping • Phenotyping • Mapping • Next-generation sequencing

1 Introduction

Plant breeding is the core area to develop genetic variations by which required traits are incorporated through selection. Traits of interest such as yield and biotic and abiotic stress resistances often are under the influence of more than one gene. Hence, to unravel the segregation pattern of such polygenic inheritance is of vital importance. The phenotype exhibited by such traits might be the aggregated action of many genes and the environment. Such assessable phenotypes have a continuous distribution pattern among individuals. The segregation pattern of such traits has previously been studied through simple statistical tools. At that time, by the involvement of the molecular markers (such as RFLPs, RAPDs, or SSRs) and visual measurement it became possible to have two types of expression (genotypic and phenotypic) of the examined individuals. Polymorphism shown by the molecular markers (genotypic variation) and through the recorded phenotypic variations compelled researchers to detect the association of genotypic variation with phenotypic patterns. To probe the segregation of required polygenic traits, biparental populations with a high number of individuals were developed. Before going into further details of such phenomena, we should know more about quantitative trait loci (QTL).

1.1 Quantitative Trait Loci

Asins (2002) reviewed that concepts of quantitative trait loci (QTL) detection had been developed from the work of Sax (1923). The acronym QTL was first coined by Geldermann (1975), reviewed by Slate (2005). The region of DNA responsible for influencing a trait that is recorded on a linear (continuous) scale is called a QTL. The expression of a quantitative trait is regulated by hundreds or even thousands of such QTLs (Mackay et al. 2009). On the basis of DNA markers positioned on a linkage map, QTLs are allotted on a chromosome in the vicinity where the statistical probability is significant. As DNA markers are not affected by the environment, after detecting their polymorphism, these can be used as a tool in mapping QTL. Quantitative traits can have varying phenotypic concentration depending upon the allelic diversity at a QTL region, and the functional markers found associated with these QTLs established the importance of QTL analysis. Thus, polygenic traits that could hardly be analyzed by the utilization of customary breeding methods could easily be labeled with DNA markers.

1.2 Essentiality of QTL Analysis

Because QTL is the region flanked by two markers (Erickson et al. 2004), it is obligatory to detect the linkage between the marker and QTL. Here mapping becomes useful, to arrange the markers, genes, or QTLs in a sequence on the

chromosome, highlighting the relative distance among them (Touré et al. 2000). When genes or QTLs linked with traits of interest are to be detected, it necessitates the construction of such maps. Without finding the association between the trait of interest and QTL, it is hard to avail the genetic diversity. By increasing the DNA marker density on the chromosome, a detailed genetic map can be produced. These maps created the importance of present-day QTL mapping (Doerge 2002). Narrowing down the distance (by increasing the number) between the markers and the QTL, a stronger linkage between marker and trait can thus be detected. The stronger the marker–trait linkage, the more authenticated the usage will be. With the help of DNA markers, it seems very important to detect the QTL linked with the trait of interest if we want to utilize that character in further breeding strategies.

1.3 Principle of QTL Analysis

QTL analysis is devised on the principle that genes and markers which segregate during meiosis, if tightly linked, must be transmitted together from parent to progeny (Collard et al. 2005). As a quantitative trait is the expression of many genes at the same time, there must be a region or locus (QTL) that if found linked with markers can thus be analyzed for further benefits. The development of a segregating population first and then the detection of marker–trait association with the help of genetic and phenotypic profiles are basic components of QTL analysis.

2 Methodology Involved

The science of quantitative genetics has been predominantly occupied by biometric mathematics. Sophisticated statistical tools are involved to extract and correlate the variation in genotypic and phenotypic diversity among individuals. QTL analysis can be performed if we have the following information:

1. A model segregating the population in which a QTL for the required trait is to be detected.
2. Genetic dissection of the population with markers.
3. A record of phenotypic variations for the trait of interest.
4. Software packages to depict marker–trait association.

2.1 Mapping Population

Breeding populations differ from natural populations because they are selected according to the breeders' interests. Based on required traits, the genetic properties of breeding population are highly confined and focused. All breeding disciplines

obey a general pattern of creating new genotypic variations. Crossing the lines with required traits has a high probability of detecting a QTL (Würschum 2012). To study the segregation of any polygenic trait of interest, parent selection is very crucial. Parents must be phenotypically evaluated and should have contrast in trait expression; for example, P1 (disease resistant) and P2 (disease susceptible). In self-pollinated species, the mapping population should be initiated from highly homozygous (inbred) parents (Collard et al. 2005). In cross-pollinated species, the F_1 generation can be developed by pair-crossing of heterozygous parent plants that are significantly different for required traits (Barrett et al. 2004). F_2 populations from F_1 hybrids, backcross-derived lines, are the usual types most often programmed for self-pollinated species and can easily be developed in a short time. Recombinant inbred lines (RILs) and doubled haploid (DH) lines are also developed. RILs and DH lines are used if homozygous lines are to be increased without any particular genetic alteration (Collard et al. 2005). In QTL mapping, construction of a mapping population must have a strategy of creating a correlation between the strength of linkage and the degree of linkage disequilibrium (Gardner and Latta 2007). Linkage disequilibrium (LD) arises when an allele at locus A is nonrandomly associated with the allele at locus B. It can befall when these two loci are unlinked (Flint-Garcia et al. 2003) (Fig.1).

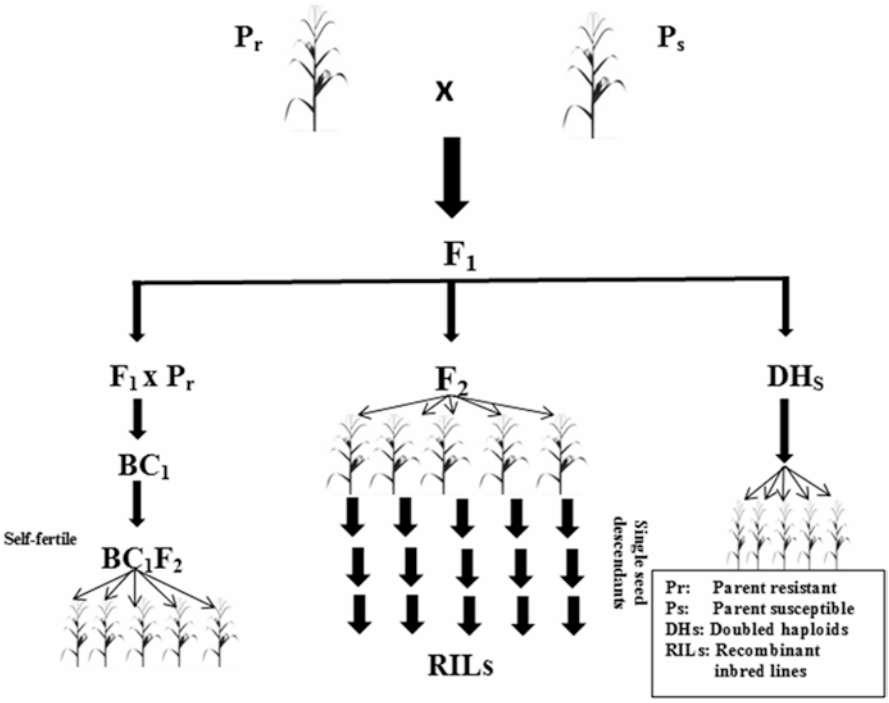

Fig. 1 Usual types of mapping population for self-pollinating species

Based on the biparental and diverse panel, there are two basic mapping approaches, that is, family mapping and population mapping. Family mapping detects only a limited number of alleles per locus at one time. Population mapping involves a diverse panel of genotypes with multiple families also, and each family with a small family size (Myles et al. 2009). The type of the population that should be used depends on the plant species, type of markers used, and the trait to be mapped (Touré et al. 2000).

2.2 Genotyping

Screening of a population along with the parents with the help of DNA markers (polymorphic) to obtain such a diversity pattern resulting from polymorphism of the markers is called genotyping (Collard et al. 2005). In the pregenomic era, populations used to be screened with a few markers of any type [restriction fragment length polymorphisms (RFLPs), random amplified polymorphic DNA (RAPDs), amplified fragment length polymorphisms (AFLPs), simple sequence repeats (SSRs), etc.], depending upon the suitability and the nature of trait segregation. The genotypic profile obtained by the marker analysis contains the number of markers used and the polymorphism shown in the population including parents. All the previous and present-day genotyping techniques have the same purpose: how fast and how many of the markers can be processed quickly. The objective of genotyping has always been to have the polymorphism indicated with few base differences underlying allelic diversity. Current aspects of genotyping are discussed in this chapter under the heading of modern perspectives. Instead of extracting and analyzing DNA from every individual of a segregating population, bulk segregation analysis can also be performed. Four DNA bulks, two from individuals of extreme phenotypes (e.g., highly susceptible and highly resistant) along with two parents are prepared. For this purpose, we need to scan the genotypes with intensive application of markers (Cheng and Chen 2010) (Fig. 2).

2.3 Phenotyping

To dissect a trait, the genotypic variation pattern shown by markers as well as phenotypic diversity display are needed. A quantitative trait that is expressed in a continuous distribution pattern is scored, and the entire population and parents are screened. This method is foremost to detect a QTL when phenotypic data must be available. The data are usually obtained by combining multiple experiments but comes with unbalanced inferences (Würschum 2012), whereas balanced data sets are found beneficial in minimizing false-positive QTLs (Wang et al. 2012). Even then the phenotypic data generated without prior balanced experimental design can also be used for QTL detection.

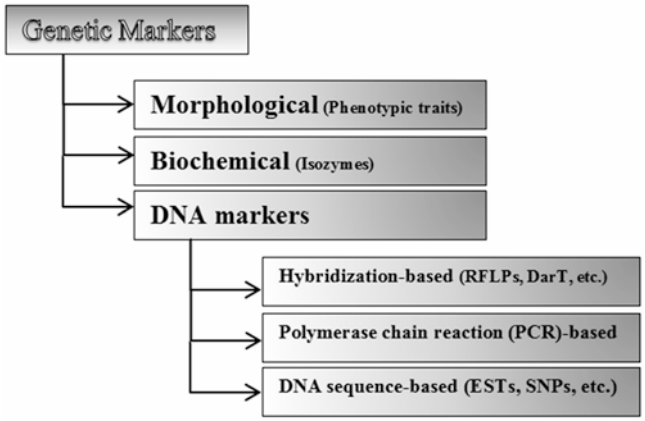

Fig. 2 Flowsheet presentation of genetic markers

Phenotyping intensity is also a notable factor for a precise QTL analysis. High heritability and low bias in the measurements are prerequisites for authenticated QTL detection (Bradbury et al. 2011; Liu et al. 2012). The obtained phenotypic profile will contain the number of individuals in a population and parents and the variation in trait expression among them. With the combination of modern approaches in phenotyping (discussed later in the chapter) and statistical tools, it has become convenient to have a more detailed and accurate pattern of phenotypic variation in the studied trait.

2.4 Software Used

After obtaining the genotypic and phenotypic picture of the mapping population, statistical tools come into use. Analysis of variance for the studied phenotypic trait in the population is mandatory. Sorting out linked loci and their strength of linkage with the phenotypic variation becomes vital. Without the aid of software packages, it seems impossible to handle the data produced by such extensive phenotypic and genotypic observations. These packages need input files that may be opened as any spreadsheet (Excel, SPSS, Statistica, SAS, Statistix, XLStats, etc.) software also. Results of marker applications and visual scoring are arranged in spreadsheet files and then formatted as the software requirements. The file format needed by the software can be found in template files of the software help manual. Most such software can be downloaded free from their respective websites along with their user manual and help files. Software that is often used in QTL mapping includes the following.

2.4.1 QTL Cartographer

QTL Cartographer is used for single-marker regression and interval mapping. It can analyze the data set obtained from F_2, inbred lines, and also from backcross-derived populations (Luciano et al. 2012). A useful software then results to be expressed in graphs. Various QTL models can be explored by generating simulation data and varying parameter settings. Rmap input and output files are used for creating linkage maps. Data files are Rcross input files and input files for QTL information are in Rqtl format in version 1.17 (Basten et al. 2004). An updated version 2.5, along with a user manual, is now also available (Wang et al. 2013).

2.4.2 MQTL

When the data set is from multiple environments, homozygous biparental progeny (recombinant inbred lines, doubled haploid lines), and the mapping is to be simple interval mapping or a simplified form of composite interval mapping, then MQTL software is the best choice. This software is specialized to handle large data sets primarily (Tinker and Mather 1995).

Nowadays there is *MetaQTL*, a Java package designed to analyze the combined data from different gene mapping experiments such as molecular markers, QTL, and candidate genes. This package is the assembly of various Java written programs executing different purposes (Veyrieras et al. 2007).

2.4.3 MapQTL

When we are concerned with experimental population of BC1, F_2, RIL, DH, and an outbred full-sib family in diploid species, then MapQTL V. 6 proves itself a user-friendly choice. For easier comparison of results from advanced backcross inbred lines, advanced intermated inbred lines, and doubled haploids derived from F_2, this software can be used. Combined analysis of multiple populations with simple experimental design along with covariance by selecting an automatic marker cofactor in a single project is the key feature of this software. Extended options for QTL chart presentation and adjustable data exportable tables are additional functions (Van Ooijen et al. 2000; Van Ooijen 2004; Van Ooijen and Kyazma 2009).

2.4.4 Joinmap

Estimation about linkage groups is the most technical task in QTL mapping. This software enables the user to study linkage group formation depending on independence test logarithm of odds (LOD) score, linkage LOD score, independence test *P* value, and recombination frequency. A linkage map can be constructed after fixing the linkage groups. With increased key components, high-quality charts to

express the maps up to the required preferences can be prepared. All the map charts can be exported to pdf format and can also be copied to MS-Word or Excel; moreover, the charts can be printed easily (Van Ooijen 2006).

2.4.5 Map Manager

Older versions of the software were Map Manager Classic, Map Manager QT, Map Manager XP, and the latest among them was Map Manager QTX (Manly et al. 2001). Map Data set from the dominant markers can also be manipulated by Manager QTX. It is modified and equipped with cross-platform libraries and designed for multiple computer platforms.

2.4.6 QGene

This software was reported by Nelson (1997) for the analysis of marker-based large amounts of genomic information in which raw genetic markers were reduced to numerical summary statistics along with prompt graphic display of both data and statistics. This software can now be downloaded from the website www.qgene.org along with its user manual. It can handle large amounts of the genotypic and phenotypic data obtained from F_2, F_3 families, BCF1, DHs, and RILs as well. A simple notepad file is prepared with marker data first; then trait data below; along with a Java Development Kit (JDK) extension. The detailed procedure is given in the user manual, and a sample data file is available with the software (Joehanes and Nelson 2008).

2.4.7 SAS

If mapping is to be performed only with single-marker analysis, then SAS is used. It can identify QTLs by detecting associations between marker genotype and phenotype of the quantitative trait. Analysis of variance, *t* test, general linear model, and regression analysis can also be performed with this package (Akbarpour et al. 2014; Rahman et al. 2014; Zambrano et al. 2014) (Table 1).

2.5 Interpreting Results

The birth of quantitative genetics was derived from the fusion of Mendelism and biometry. The combination of molecular genetic techniques and powerful statistical methods enables the researcher to dissect the complicated quantitative traits (Mauricio 2001). After having the detailed and authenticated genotypic and phenotypic profiles of all the individuals of a segregating population and the parents

Table 1 Computer software used in quantitative trait loci (QTL) mapping

Plant species	Software	QTL	Reference
Cotton	Join map	65	Tang et al. (2015)
Peanut	QTL Cartographer	mQTL	Pandey et al. (2014)
Brassica oleraceae	MapQTL v.4	13	Lv et al. (2014)
Potato	Illumina software	mQTL	Prashar et al. (2014)
Grape	MapQTL	3	Ban et al. (2014)
Vicia faba	Map manager v. 20	4	Kaur et al. (2014)
Yellow croaker	Join map	7	Ye et al. (2014)
Rice	WinQTLCart. v. 2.5	3	Yun et al. (2014)
Maize	QTL Network v. 2	55	Liu et al. (2014)
Eggplant	QGene	71	Frary et al. (2014)
Wheat	SAS v. 8.1	4	Daoura et al. (2014)

involved, the need to analyze the results is fulfilled by the computer software. Hence, comprehensive interpretation is necessitated. The following details are mandatory to understand and interpret the results.

2.5.1 Isolation of Linked Markers

Linkage analysis for a high number of markers cannot be done manually. With the help of computer software, as already mentioned, linkage can be determined using odds ratios. Understandable expression of this ratio as the logarithm is based on the hypothesis that among the total number of markers how many are linked and the rest are unlinked. So, the logarithm of odd ratios is "the ratio of linkage versus no linkage" (Collard et al. 2005). A logarithm of odds (LOD) value greater than 3 is usually applicable for mapping. If any two markers have a LOD value of 3, the chances of their linkage is more than 1000:1 (linkage:no linkage). LOD is basically a *Z*-distribution (Morton 1955).

$$\begin{aligned} \text{LOD} = Z &= \log_{10}\left[\begin{array}{l}\text{Probability : that two markers are linked /}\\ \text{Probability that two markers are unlinked}\end{array}\right] \\ &= \log 10\left(1-\theta\right)^{\text{NR}} \times \theta^{R} / 0.5^{(\text{NR}+R)} \end{aligned}$$

where LOD is the logarithm of odds, θ is the recombinant fraction $= R/(\text{NR}+R)$, NR is the number of nonrecombinants, and R is the number of recombinants.

For large data sets, LOD can easily be calculated by the software mentioned. As many as the number of individuals in the population, the authenticity for determination of genetic distance between the markers and their sequence will be increased (Collard et al. 2005).

2.5.2 Mapping Function

This function It is required to convert a recombination fraction to the centimorgan (cM). It has been observed that recombination frequency and crossing over are not related in a linear order (Hartl and Jones 2001). Mapping function is also calculated by recombination values. Mapping functions are mathematical adjustments used in the measurement of genetic distances between two loci (Vinod 2011). Vinod (2011) has also emphasized that there are three options, to choose any of the three of the mapping functions:

- Complete interference does not permits double crossover; thus, Morgan's mapping function is there to be applied to cover additives.
- Incomplete interference enables double crossover to a certain extent, so we have Kosambi's mapping function to be used.
- No interference compels us to use Hadan's mapping function.

The genetic distance between the markers or genes is not directly related to the physical distance on DNA between genetic markers but also corresponds to the genome size of the plant species (Han and Ming 2014). As we know, markers split the mapping population into different clusters. Then, we have two types of grouping, one made by the markers and the other made by the visual observation of a continuously varying trait. We also have information about the linked markers. The statistical significance between the groups made by the markers and phenotypic trait means is then of prime importance (Young 1996).

2.5.3 Single-Marker Analysis

The single-marker effect can be analyzed statistically by *t* test, analysis of variance, and linear regression. Coefficient of determination (R^2) from the marker that explains the variation shown by a quantitative trait describes to what extent the marker and the QTL are linked to each other (Collard et al. 2005).

2.5.4 Interval Mapping

Sometimes an issue faced after single-marker regression is the effect of QTL magnitude and position (Erickson et al. 2004) and is resolved by the interval mapping techniques. It confines the QTL between the interval of a pair of two genetic markers with the help of a LOD (maximum likelihood) score (Collard et al. 2005). With the help of the interval, the mapping effect between the QTL and marker distance is expressed as a magnitude. Interval mapping is mainly of four types: simple interval mapping (SIM) as performed by Nelson (1997), composite interval mapping (CIM) (Basten et al. 2004), and multiple interval mapping (MIM) by Zeng et al. (1999).

The results obtained can be presented in a tabular form including highly linked markers or by graphs made by software (Burton et al. 2014, 2015; Oakley et al. 2014).

3 Modern Perspectives in QTL Analysis

With every passing day, progress is made in each field of the sciences as in electronics equipment, software packages, and chemical sciences. Traditional QTL mapping with respect to phenotyping and genotyping has been modernized as well. By the advances in genotypic and phenotypic platforms, it has now become possible to perform multi-trait analyses to unravel pleiotropy and the gene control mechanisms of complicated traits (Alonso-Blanco and Méndez-Vigo 2014).

The search for genetic polymorphism by using intensive and a variety of markers for a particular species always opens the door for detailed and modified phenotyping, which is helping breeders, plant pathologists, and physiologists as well. Having detailed genotypic information, it has become feasible to check the association of phenotypic diversity with new genetic regions. Understanding of genetic and molecular bases of polygenic traits has always been the major objective of the geneticists. As much as the loci are involved in controlling a particular trait, to detect their interaction and interference becomes vital, demanding a high level of specialization.

Meta-analysis of QTL mapping is a promising tool in which multiple quantitative trait loci are analyzed. Results obtained from different studies demand more statistical potential for QTL identification. Thus, meta-analysis can produce stronger inferences than other univariate studies. Details of the meta-analytical aspects of QTL have been a focus by Wu and Hu (2012). Possibly the genetic bases of quantitative traits are related to phenotypic level, which also fluctuates between simple oligogenic and complex polygenic inheritance (Joseph et al. 2013).

3.1 Genotyping to Genomics

For QTL analysis, much detail about genotypic variations is available so as to better analyze the QTL responsible for the trait of interest. In the present day, screening of a mapping population with only a few hundred markers has now been shifted up to 9K, 90K iSelect SNP (Avni et al. 2014). DArtT markers (Grzebelus et al. 2014) kits are also available, and genotyping by sequencing (GBS) is another platform to assess genetic diversity among the segregating population individuals (Verde et al. 2012; De Donato et al. 2013; Buckler 2014; Larson et al. 2014; Liu et al. 2014).

To detect single-nucleotide polymorphisms (SNPs), there is the widely adapted technique known as microarray technology that identifies SNPs through hybridization of DNA to oligonucleotides fixed on a chip. This microarray-based genotyping

detects allelic diversity by locating thousands of SNPs quickly (Huang and Han 2014). Five high-throughput genotyping methods have been reviewed by Huang and Han (2014): microarray-based genotyping, sequencing-based genotyping, genotyping-based sequencing, RNA-seq-based genotyping, and exon-sequencing-based genotyping.

As a crop reference genome is published, it become easier to characterize genome-wide variation for genetic mapping (Lai et al. 2010; Jiao et al. 2012).

3.2 Phenotyping to Phenomics

Large numbers of quantitative traits have been traditionally dissected at different levels of biological organization, not only because of details provided by advanced genotyping platforms but also simple to modern phenotypic techniques. The shift from phenotyping to phenomics is characterized by measurement of physical and biochemical traits of the organism as they respond to genetic diversity and environmental fluctuation. High-throughput 2D and 3D image analyses are being used to produce a phenotypic profile for QTL analysis (Topp et al. 2013; Joosen et al. 2012). Fieldwork for phenotyping is still very difficult, particularly when experimental crops have been planted on multiple environments in a vast area. Presently, some sensor-based platforms have been made for measuring biomass traits. Near-infrared spectroscopy on agricultural harvesters and spectral reflectance of plant canopies reflecting that future development in phenotyping will enables QTL analysis to be more detailed and widely applied in the gene discovery of food crops (Huang and Han 2014).

In phenotype cover interface between the genome and the environment, the phenotypic architecture is often equipped with an explained set of biodiversities (Burleigh et al. 2013).

3.3 Multiparent Advanced Generation Inter-Cross (MAGIC) Populations

MAGIC populations were first reported by Mott et al. (2000), and further development of such populations was performed by Kover et al. (2009) when it was hypothesized that QTL can be analyzed with improved accuracy along with cloning. A first panel of MAGIC lines with a set of 527 RILs of *Arabidopsis thaliana* was produced. Many known QTL with high precision and some important QTL for germination data and bolting time were detected. It has been recommended that the usage of MAGIC lines for other organisms can analyze QTL with more authenticity. QTL analysis using MAGIC lines using the probability of inheriting founder alleles across the whole genome at a time, and the whole-genome approach was estimated during a simulation study and proved itself a powerful method of analysis (Verbyla et al. 2014).

3.4 Next-Generation Sequencing (NGS)

NGS is a high-throughput sequencing-based genotyping technique. NGS technology is being widely adopted in which millions of DNA fractions at a time are being synthesized and sequenced. A genomic DNA sample is sliced into a library of small fragments that are uniformly and exactly sequenced in millions of parallel reactions. Newly detected lengths of bases, which are then called reads, again reunite using a known reference genome, and the full set of arranged reads represents the entire sequence of each chromosome (Grada and Weinbrecht 2013). Quail et al. (2012) compared three major sequencing platforms (Torrent's PGM, Pacific Bioscience RS, and the IlluminaMiSeq) with IlluminaHiSeq and concluded that all three fast turnaround sequencers were able to generate usable sequences but that crucial differences were found among the quality of the data.

Burleigh et al. (2013) purposed a next-generation phenomics project to facilitate biologists working with phenotypic data. Three prominent areas have been focused: (a) computer vision techniques to detect and record trait, (b) to increase the speed of the scoring and producing data sets supported with labeled anatomical images, and (c) to extract character data, natural languages will be processed.

NGS technologies offering latest moves toward fine-mapping as well as gene identification are greatly beneficial for food crop research. Trick et al. (2012) employed bulk segregant analysis (BSA) to fine-map the genes in tetraploid wheat lines and discovered SNPs with the help of next-generation sequences data.

4 Practical Potential of QTL Analysis

Mineral nutrition along with micro and trace elements (Lowry et al. 2012), primary and secondary metabolites (Joosen et al. 2013), and some flavonoids influencing quantitative traits have been studied in recent years (Routaboul et al. 2012). QTL analysis has explored certain levels of transcriptomic field encompassing transcript variations. Cubillos et al. (2012) while studying the RILs of *Arabidopsis* stated that genetic makeup that is responsible for transcriptional variation can assist knowing the phenotypic variation. During the study of epigenetic variations, a new class of methyl QTL has also been reported by Schmitz et al. (2013). Differentially methylated regions (DMR) have also been mapped and depict that a major part of such epigenetic quantitative variations is the consequence of genetic variation in *cis*-methyl QTL and *trans*-methyl QTL. Alonso-Blanco and Méndez-Vigo (2014) reviewed that DMRs are found associated with gene expression variation; hence, it can be assumed that methyl QTL are about to display another molecular level controlling expression and ultimately a higher level of quantitative traits. Differential QTLs for micronutrients in seed structure have also been reported by Blair et al. (2013). Moscou et al. (2011) detected a *cis*-eQTL gene as candidate for a major fungal resistance locus as well as *trans*-eQTL colocating with an enhancer of the resistance (reviewed by Alonso-Blanco and Méndez-Vigo 2014).

4.1 Crops with Improved Breeding Strategies

In crops, to dissect complex QTLs such as grain yield and stress tolerance, a huge sample size up to thousands of individuals is required. Now it has become possible to genotype such large samples using advanced genotypic methods. Crop breeding based on Marker-assisted selection is beneficial for simple Mendelian traits, but it is trouble creating for complex quantitative traits such as stress tolerance. Sometime through marker-assisted selection an unexpected QTL appear and fails in trait expression with little phenotypic variation being observed. Such trouble shoots can be overcome through genomic selection. Genomic selection is a simple and powerful approach in which breeding values are assigned using their phenotypes and marker genotypes (Deshmukh et al. 2014). By applying molecular breeding techniques, food crops such as maize, rice, potato, and wheat have been greatly advanced and developed with respect to their yield and stress tolerance.

4.2 Revealing the Genetic Bases of Abiotic Stress Tolerance

Abiotic stresses such as drought, heat, and salinity have massive influence on food crop yield. Mechanism of abiotic stress tolerance and exact phenotyping for such aim has been poorly formulated so far. Irrespective to the constant and single environment, a number of QTLs under the influence of environmental interaction has been identified so far. Studies such as germination, growth, and flowering time are being performed under variable field conditions of temperature and moisture in different environments (Fournier-Level et al. 2011; Ågren et al. 2013; Leinonen et al. 2013). Crops having ability to adapt extreme environmental conditions can be a significant source for crop improvement to fulfill the food needs of the ever-increasing populace (Huang and Han 2014). An abiotic stress tolerance mechanism can be traced out with phenomics and genomic tactics. Molecular bases of environmental tolerance are being probed through high-throughput phenotyping and genotyping platforms (Roy et al. 2011).

For drought tolerance, a QTL hotspot has been reported during the study of three populations in maize (Almeida et al. 2014). Constitutive and adoptive regions for drought tolerance were earlier reported by Almeida et al. (2013). Doubled haploid (DH) lines of canola were examined to associate root and leaf traits with drought tolerance with the help of QTL analysis (Mekonnen 2013). A high-throughput phenotyping platform has been used to identify drought tolerance QTL in wild barley introgression lines (Honsdorf et al. 2014). Using SNPs and haplotypes, QTL for height and biomass as secondary traits of drought tolerance were detected in maize by Lu et al. (2012).

Using SNPs, QTLs for heat tolerance in rice have been mapped by Ye et al. (2012). Paliwal et al. (2012) mapped QTLs on 7DS in hexaploid wheat using the composite interval mapping approach. Talukder et al. (2014) mapped QTLs for the

traits responsible for heat tolerance in wheat. Family-based QTL mapping of heat tolerance in *Triticum turgidum* has been performed by Ali et al. (2013).

As far as salt tolerance is concerned, QTL mapping has been performed in a variety of valuable crops to make the optimal use of saline or salt-affected lands. Chankaew et al. (2014) mapped QTLs for salt resistance in *Vigna marina*. In *Zoysia japonica* QTL analysis was performed by (Guo et al. 2014). Validation of the dominant salt tolerance gene in cultivated soybeans was mapped by Guan et al. (2014). In wild soybean, a major salt tolerance QTL was mapped by Ha et al. (2013).

4.3 Exposing Genetic Dissection of Biotic Stress Resistance

Stress resistance mechanisms are governed by many genes in most plant species. Plant–pathogen interactions underlie the effect of many genes responsible for plant defense. QTL analysis successfully helps in genetic dissection of the resistance mechanism. After detecting the QTL region involved in biotic stress resistance, marker-assisted selection enables the breeder to produce more resistant crops. QTLs for disease resistance found and utilized in breeding create durable resistance in genotypes, which proves an active method to achieve such broad-spectrum resistance, and thus these modified crops can be a good genetic resource (Kou and Wang 2010).

By using the marker-assisted selection (MAS) approach, gene pyramiding is performed to create broad-spectrum resistance in plant species (Tester and Langridge 2010). MAS for Lr 34, Yr 18, and powdery mildew 38 resistance in wheat and barley have been performed by Miedaner and Korzun (2012). Joshi and Nayak (2010) reviewed that durable stress resistance in crops can be achieved through gene pyramiding. Gene pyramiding for rice blast management through host-plant resistance has been reported by Sharma et al. (2012). To avail the gene pyramiding technique, Grimmer et al. (2014) analyzed four different wheat mapping populations being segregated for partial resistance to four contrasting foliar pathogens. It was stated using simple multiplicative survival (SMS) that with an increased number of loci, an enhanced level of disease resistance was achieved in wheat lines. In rice, quantitative resistance genes *pi21*, *Pi34,* and *Pi35* have been pyramided by Yasuda et al. (2015). Rice breeding lines with three pyramided resistance genes have been developed for broad-spectrum resistance against bacterial blight (Suh et al. 2013).

One major QTL for leaf spot and rust resistance in groundnut has been reported by Khedikar et al. (2010). In wheat, QTL mapping for multiple foliar disease and root lesion nematode resistance has been focused by Zwart et al. (2010). In potato, working on late blight resistance, a consensus map and QTL meta-analysis were performed by Danan et al. (2011). Genome-wide association mapping revealed disease resistance QTLs in barley (Gutiérrez et al. 2013). QTL mapping for fruit rot resistance in a *Capsicum annuum* population was done by Naegele et al. (2013).

A massive literature has become available in recent years to highlight the significance of QTL analysis. Here we present one view of a survey in table form (Table 2).

Table 2 Trends in QTL analysis in plants

Plant species	Type of population	Trait studied	QTL/method	Markers	Reference
Peanut	BC derived	Flower color, growth habit	Chi-square	115 SSRs	Fonceka et al. (2012a, b)
Cotton	RILs $F_{6:8}$	Fiber quality	50 QTLs CIM	5742 SSRs	Sun et al. (2012)
Maize	RILs	Kernel quality	26 QTLs	GWAS	Cook et al. (2012)
Peanut	BC derived	Yield components	95 QTLs SIM	SSRs	Fonceka et al. (2012a, b)
Wheat	RILs	Seedling traits	380 QTLs	SSRs	Guo et al. (2012)
Eggplant	156-F_2 plants	Anthocyanin contents	6 QTLs Interval Map.	SNPs, RFLPs, COSII	Barchi et al. (2012)
Wheat	RILs	APR Ug99	QTL on 7AS 2,3BS,5BL,	DArT	Singh et al. (2013)
Peach	126-F_1 Plant	VOCs, pest resistance	72 QTLs	SNPs, SSRs	Eduardo et al. (2013)
Rice	NILs BC_5F_4	Grain wt. Panical spike	QTLs	SSRs INDELs	Luo et al. (2013)
Grapevine	Pseudo F_1 Progeny	Skin color	eQTL	Transcript	Huang et al. (2013)
Sesamum indicum L.	P1, P2, F1, F2 BC1, BC2	Seed coat color	4QTLs CIM	653 SSRs AFLPs, RSAMP	Zhang et al. (2013)
Zoysia grass	120-F1	Salt tolerance	3QTLs Interval Map.	217-SRAP 25-RAPDs	Guo et al. (2014)
Capsicum annum	RILs F_6	Fruit rot resistance	QTLs	High-density Map.	Naegele et al. (2014)
Maize	RILs 3-populations	Root anatomical traits	6QTLs	Map used	Burton et al. (2014, 2015)
Eggplant	F2	Agronomic traits	7QTLs Interval Map.	Map used	Portis et al. (2014)
Wheat	RILs 3-populations	Yield traits	165 QTLs	DArT	Cui et al. (2014)
Rice	RILs	Seed vigor	8QTLs	Map used	Xie et al. (2014)
Soybean	304-Short season lines	Agronomic traits	GWAS	GBS	Sonah et al. (2015)

5 Conclusions and Future Perspective

From the Mendelian era to Morgan's linkage analyses, extension of knowledge from qualitative traits to quantitative, it has become clear that in days to come nucleotides and their expression will be comprehensively understood. Fine mapping, chromosome walking, and dissection of the quantitative traits with the help of highly dense maps has annexed genetics with all other biological sciences. To see genetic change and diversity has now become very clear with the aid of next-generation sequencing platforms. With the passage of time, the science of genetics is becoming laboratory based, but to the common man the threat of hunger and starvation still prevail with the increasing populace. What has been done in the field of molecular breeding has not yet advanced the contribution of the green revolution: even at that time such sophisticated tools were not available. Now with the advances in laboratory science there comes a dire responsibility to the agricultural researcher to feed the world populace of more than 9 billion in coming years. Can such fancy laboratory techniques fill the empty stomachs of nutritionally deprived peasants? There is a need to integrate laboratory science with fieldwork and to target it as per the demands of the market and common people. Such research should have an impact rather than being an impact factor.

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