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QTL Analysis in Rice Improvement: Concept, Methodology and Application

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Abstract: Plant breeding is the management of genetic variability. A large number of traits of economic importance are quantitative in nature and are characterized by continuous variation owing to large number of genes governing them. Advances in molecular biology have helped to dissect these traits into finer details but we are still far from precise location and enumeration of the genes conditioning a quantitative trait. Various aspects of study of quantitative traits are number of genes, chromosomal locations, allelic and non-allelic interactions, G x E interaction and pleiotropy effects. QTL mapping is an integration of linkage mapping and traditional statistical and quantitative genetic approaches. Various methods of QTL mapping such as single marker analysis, interval mapping, composite interval mapping and multi trait mapping have been standardized using several mapping populations such as F2, back cross, RIL's, NIL's and double haploids and various software packages. A large number of QTL's have been identified for various economic traits which account for a sizeable proportion of the genetic variation and as such is turning out to be more than just a statistical inference. Advances in QTL mapping will help in genetic analysis of complex traits, plant genomics, germplasm enhancement, improved selection efficiency through MAS and studying gene expression along growth and developmental phases of plant life.

Key words: Rice, quantitative trait, QTL mapping, mapping populations, single marker analysis, interval mapping, composite interval mapping, marker aided selection

INTRODUCTION

The success of plant breeding operations exclusively relies on genetic variation. In fact plant breeding uses selection for improving plant architecture for traits of economic and agronomic importance by using genetic variability. In crop plants a greater proportion of such traits are governed by a large number of genes with smaller contributions to the trait resulting in continues rather than discrete variation (Liu, 1998). Even traits considered to be more simply inherited, such as disease resistance, may be actually quasi-qualitative for which trait expression is governed by several genes i.e., major genes plus several modifiers (Stuber *et al*., 1999). Thus the trait values are measured rather than counted. The analysis of such quantitative variation especially its potential genetic basis is of prime importance to a plant breeder (Asins, 2002). Because of their features such a large number of genes, small effects and greater vulnerability to environmental influences. Their phenotype does not provide ample insight into their genotype as against simple monogenic traits (Kearsey, 2002).

Fisher (1918) was first to provide an understanding of quantitative traits and their measurement. Even upto 1980's, the genetics of such traits was studied by using simple statistical techniques (means, variances, co-variances, heritabilities etc.). The assumption underlying such techniques was that there are several genes segregating in a given population and that these genes would share individual allelic contributions which are slight relative to environmental contribution. Even on such a minimalistic or black box concept, considerable progress was made in advancing our knowledge of nature and effect of quantitative inheritance. Considerable theoretical and experimental progress has been made in understanding various aspects of quantitative traits such as heritability, direct and correlated response to selection and subsequently optimizing the breeding methodologies for improving upon a crop species (Kearsey, 2002). There are, however, obvious limitations to understanding of nature of QT's because of lack of discrete phenotypic segregation and because genotype effects of each gene associated with a complex trait are relatively small.

The advances in biometrics has made it possible to study QT's in finer details. However, these advances only

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help in measuring the effect of a group of genes in terms of means, variances and covariances. The precise nature of individual gene action conditioning a quantitative trait is still far from adequate, the most important hindrance arising due to small phenotypic effects of such genes and the actual number and position cannot be precisely determined. This greatly hampers their cloning and possible use in development of transgenics for quantitative traits.

For getting an insight into the nature of quantitative traits and the genes governing them, one needs to have proper understanding of following aspects.

- Number of genes
- Chromosomal locations of these genes
- Nature of distribution effects-major and minor effect genes.
- Nature of allelic and non-allelic interactions like dominance, epistasis etc.
- Nature of G x E interaction-variation of expression over environments.
- Nature of genes-regulatory/structural through genomic studies
- Plicotropy effects

The integration of biometrical and molecular techniques have made it possible to explore the nature of QT's by mapping of QTL (Quantitative Traits Loci). Given the advances in genomic research and computer simulation techniques, it is now possible to identify, locate and clone gene groups, constituting a QTL. A number of molecular marker systems such as RFLP, AFLP, SSR (microsattelites), SNP etc coupled with a number of advanced computer packages such as QTLS/MAPMAKER (Lander *et al*., 1987), QTL STAT (Knap *et al*., 1992), LINKAGE (Terwilliger and Qtt, 1994) and Map Manager QT (Manly and Cudmore, 1996) have made it possible to construct high density maps wherein QT's can be associated with markers by analyzing data from different populations such as F2, F3, Backcross (BC), Double Haploids (DH's), Recombinant Inbred Lines (RIL's), Near Isogenic Lines (NIL's), Backcross Inbred Lines (BIL's) and several mutants.

QTL's and QTL mapping: QTL's are loci controlling quantitative traits. Any chromosomal region associated with a QT and a marker is defined as QTL (Xu, 2002).

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I--------------------I------------------------I----------------------I
   Marker A              QTL                    Marker B
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QTL mapping is a combination of linkage mapping and traditional statistical and quantitative genetics approaches using parameters such as variances to elaborate quantitative traits at individual gene level in order to draw inferences at population level. QTL mapping is essentially a set of procedures aimed at first detecting and then locating a QTL. The concept of detecting QTL's was first elucidated by Sax (1923). The first known statistical approach was proposed by Thoday (1961). Advances in Molecular genetics have now enabled us to detect at least some of the genes or genomic regions conditioning a quantitative trait. Thus QTL mapping essentially includes detection and locating a QTL and analyzing certain fundamental aspects like, number, nature of gene action and effects, epistasis, plieotrophy and QTL x E interaction.

Basic problems in QTL analysis: The problem of identifying the genetic factors underlying complex and quantitative traits has a long history (Sen and Chirchill, 2001). The basic approaches used for accurate location of genes using certain populations described earlier coupled with the advances in molecular genetics have resulted in identification of a large number of QTL's through their association with specific markers during meiosis (Kearsey, 2002). Even though such techniques have been greatly standardized to ensure a fair level of precision, yet they suffer from certain problems arising out of complexity of quantitative traits besides statistical errors. A few of the basic problems in QTL analysis are elucidated below.

- Large confidence intervals of upto 5 to 30 cM, arising out of lack of recombination at meiosis (Guo and Lange, 2000). It has been found that upto 80% of chromosomes survive meioses with one cross over or none. Thus it needs a large sample to be analyzed in order to have enough cross-over to help detect a QTL. The size of sample is further inflated by low heritability of quantitative traits. Using large populations and several generations of random mating are solutions to this problem but both of them are invariably impracticable.

  The basic implication of large C.I's is that even a 10 cM interval will contain about 130 genes in rice, which makes it very difficult to identify a candidate gene with precision.
- Another basic problem in precise QTL location is the true number of QTL's governing a quantitative trait (Hyne *et al*., 1995). It has been found that it is difficult to locate more than 12 QTL's in a given population at one time. Moreover because only significant effects are reported, the effects will be biased towards larger value. The bias will be more

with stringent significance levels because only larger effects will turn out to be significant. Besides the bias is more in case of dominance effects than additive effects as the former are relatively difficult to be detected. Thus what comes out at the end is underestimation of true number of QTLs with overestimation of their additive and dominance effects.

- It is not possible to distinguish between two QTL's that are <20 cM apart (Kearsey, 2002). The immediate implication is that no QTL will be detected when they are in repulsion phase linkage or a large ghost QTL being put in place between two true QTL's when they are in coupling phase. This greatly interferes with precise location and size of QTLs.
- Statistical methodology used for QTL mapping to detect the possible presence of a QTL at a given position use certain critical values for probability level. Sometimes two many false QTL's can be detected. Sample size in any statistical procedures has also a strong impact on QTL analysis (Asins, 2002).
- QTL's like other genes may be environmentally sensitive. When experiments are conducted over environments, QTL x E interactions may arise. These interactions oftenly get confounded with main effects of a QTL. The immediate implication of QTL x E interaction is inconsistency in detection of QTL's across environments. However, Jansen *et al.* (1995) proposed that failure to detect a QTL across environments does not necessarily mean QTL x E interaction but may be due to sampling or experimental error, because the probability of detection of QTL in multiple environments is small. Further, detection of QTL across environments does not rule out QTL x E interaction because QTL x E_{ij} terms in QTL analysis of shared QTL's were significant in a rice D H population in two different environments (Yan *et al.*, 1999).

The genetic basis of QTL x E interaction is mainly the differential gene expression. Li *et al.* (2003) concluded from their studies on QTL x E interactions in rice on plant height and heading date, using DH lines from IR-64 and Azucena that there are three aspects of QTL x E interaction

- A QTL expresses in one environment but not in another, as reflected in inconsistent detection of QTL across environments.
- A QTL expresses strongly in one environment but weakly in other, as reflected by significance of QTL x Eij term for shared QTL's.
- A QTL expresses very differently and has opposite effects in different environments.

Following table shows the inconsistency of QTL sharing across environments using same populations.

Trait	No. of QTL	Shared	References
Yield	15	2	Yu *et al.* (1997)
Panicle per plant	7	3	Yu *et al.* (1997)
Grain per plant	16	4	Yu *et al.* (1997)
1000-grain weight	17	9	Li *et al.* (2000)
Drought avoidance	21	2	Courtios *et al.* (2000)
Flood tolerance	12	3	Sripong *et al.* (2000)
Aluminium tolerance	4	2	Wu *et al.* (2000)
Disease resistance	17	7	Tang *et al.* (2000)
Seedling vigour	13	3	Redona and Mackill (1996)
Paste viscosity	7	2	Bao *et al.* (2000)

QTL mapping: The fundamental basis of QTL mapping is the relationship of quantitative traits with qualitative traits. These traits used to detect and locate QTL's are called as markers. Owing to specific advantages, genetic markers have been the torchbearers, whose mode of inheritance and genome locations can provide us an insight into the understanding of loci controlling quantitative traits. Thus in our attempt to map the QTL's, we follow the inheritance pattern of markers that are tightly liked to the QTL. The basic assumptions underlying QTL mapping are (Liu, 1998).

- Genes controlling QT's can be mapped on genome like genetic markers because of their proximity.
- Since genetic markers are interspersed throughout the genome of higher plants, there are possibilities that a sizeable proportion of these markers may be linked to quantitative trait loci.
- Since markers and the QTL co-segregate in a genetically defined population, the linkage relationships can be established by comparing the variation in the trait and the segregation pattern of genetic markers.

The mathematical model to analyse the association between a trait and marker is given by following equation:-

$Yj = \mu + f(\text{marker } j) + Ej$, where
Yj = Trait value of J^{th} individual in a population.
μ = Population mean.
f (Marker) = Function of genetic marker
Ej = Residual error associated with J^{th} individual

Mapping population: A number of population as described already form the basic material for QTL mapping. Various such populations and their origin have been shown in the Fig. 1 (Cowen, 1988).

Most QTL analyses in plants use populations derived from purelines, using several approaches to associate a marker with a QTL in such populations (Kearsey and Pooni, 1996). In autogamous species like

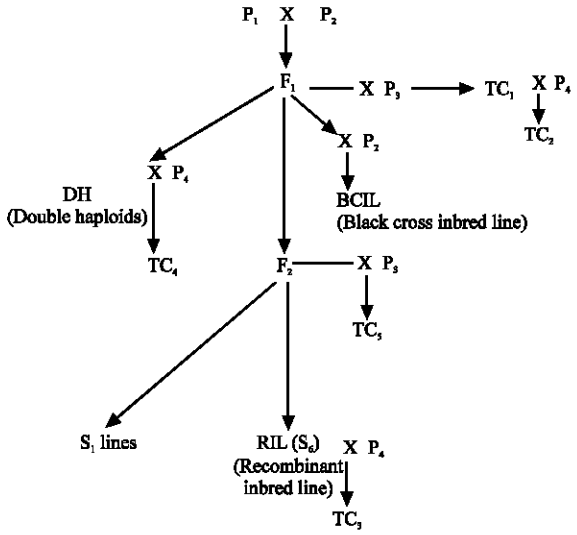


Fig. 1: Various mapping populations and their scheme of development

rice, mapping studies frequently make use of F_2 or Backcross generations because they are easiest and earliest to obtain (Asins, 2002). An F_2 is better than Backcross since a QTL with recessive alleles in a recurrent parent, BC gives biased estimates because additive and dominance components are completely confounded. However, F_2 and Backcross have inherent inconveniences of use because they cannot be replicated several times and epistatic component can not be studied. These problems are overcome by use of Double Haploids (DH's) or Recombinant Inbred Lines (RIL's) which have further advantage of small sample requirement and fever individuals to be screened. Moreover, more accurate estimates of location or QTL can be obtained with less variance. However, the power of detection of QTL in DH's or RIL's depends upon the heritability of a trait. For a given type of gene action, DH's are as good as F_2, but if dominance is present DH's and RIL's can detect only additive component (Asins, 2002).

In most of experimental designs aimed at detection of linkage between a set of genetic markers and QTL's, individuals of a population of interest are scored for that set of markers and evaluated for QT'S of interest (Cowen, 1988). There are main effects, within population dominance effects and dominance effects relative to an allele in unrelated inbred line.

Linked main effects can be evaluated by S_1, DH or RIL. Main effects are most easily detected using DH lines. Both DH and RIL's are better than S_1 lines. RIL'S usually take a long time for development than S_1 or DH. S_1's have additional advantage of allowing detection of linked main effects as well as within population dominance.

Table 1: Expected ratios of dominant and codominant markers in F2, BC and RIL populations

Population	Codominant loci	Dominant loci
F_2	1:2:1	3:1
Backcross	1:1	1:1
RIL	1:1	1:1

Each of the mapping population will give a specific segregation ratio at each locus. The knowledge of these ratios is important to determine if the population is expressing a skewed segregation ratio at any locus. The expected ratios at each locus for co-dominant and dominant markers segregating in three types of populations are presented in Table 1.

Once segregating populations are analysed by biochemical (Isozymes) or genetic (RFLP, RAPD etc) markers and it is found that segregation ratio at each locus does not deviate from expected ratio, the process of developing the map begins. The data is compiled and used to derive the linkage relationship among markers.

Lander and Botstein (1989) presented a classical approach of QTL mapping using Backcross populations. According to their approach, if we assume two inbred lines A and B differing substantially for a QT and if BC_1 is the backross with A as recurrent parent. Let (μ_A, σ^2A), (μ_B, σ^2B), (μ_{F1}, $\sigma^2 F_1$) and (μ_{BC}, σ^2BC), are means and variances of A, B, F_1 and BC_1, respectively and if $D = \mu_B - \mu_A = 0$, then assuming complete co-dominance and no epistasis,

$$\mu_{F1} = \tfrac{1}{2}(\mu_A + \mu_B)$$
$$\mu_{BC} = \tfrac{1}{2}(\mu_A + \mu_{F1})$$
$$\sigma^2A = \sigma^2B = \sigma^2 F_1 < \sigma^2 BC_1$$

The variances within A, B and F_1 equal environmental variance σ^2E (because they are genetically identical) whereas variance within BC_1 also includes genetic variance;

$$\sigma^2B = \sigma^2G + \sigma^2E$$
$$\text{or} \quad \sigma^2G = \sigma^2BC + \sigma^2E$$

The phenotypic effect of QTL (δ) is given by the additive effect of substituting both A alleles by B alleles. A single allele has effect equal $\frac{1}{2}\,\delta$, since additivity is assumed. In BC generation, segregation effect of QTL with effect δ contributes $\delta^2/16$ to genetic variance σ^2G. Thus the variance explained by a QTL is

σ exp. = $\delta^2/16$ and the residual variance is
σ^2 res. = $\sigma^2BC - \sigma^2$ exp.

Wright (1968) proved that the number of QTL's segregating in a BC between two inbred lined with phenotypic effect D is:-

$$K = D^2/16\,\sigma\,G$$

Assuming that,

- QTL's have effects of equal magnitude.
- QTL's are linked.
- Alleles in high strain increase the phenotype and those in low strain decrease the phenotype.

The variances explained by a single QTL is σ^2 exp = $(D/K)^2/16$ and the total genetic variance explained by K QTL;s would be $\sigma_G^2 = (1/K)(D^2/16)$.

The quantity K is called as number of effective factors. If the above assumptions hold true, then each QTL affects phenotype by a ratio (D/K) and explains 1/K of genetic variance (Lander and Botstein, 1989). However, all above assumptions are not satisfied always (Paterson *et al*., 1988) and consequentially the number of effective factors (K) is underestimated. In principle, the number of QTL's is unlimited. However, in case of violation of above assumptions, the number of QTL's is seriously underestimated. Despite specific advantages, the number of effective factors may not be a realistic estimate of number of QTL's.

Single marker analysis of QTL detection: The traditional approaches of detecting a QTL in proximity of a genetic marker (Sax, 1923; Soller and Brody, 1976; Tanksley *et al*., 1982; Edwards *et al*., 1987) involves comparison of phenotypic means of two classes of progenies. Those with a marker genotype AB and those with AA (Lander and Botstein, 1989). The difference between two means provides an estimate of phenotypic effect of substituting B allele for A allele at QTL. The testing is done by a single one-way ANOVA amounting to linear regression. The traditional approaches suffer from following discrepancies.

- If the QTL does not lie at marker locus, its phenotypic effect is seriously under estimated. With recombination fraction r, the downward bias in phenotypic effect of QTL is (1-2r).
- If the QTL does not lie at marker locus, the number of progeny to detect it is substantially increased. For an RFLP map with markers at every 10, 20, 30 or 40 cM throughout genome, the progeny required increases by 22, 49, 82 and 123%, respectively. The number of progeny required for detection of QTL is given by (Soller and Broady, 1976).

$$N = (Z\lambda)^2\,(\sigma^2\,res/\sigma^2 exp)$$

When σ^2 exp decreases, N increases.

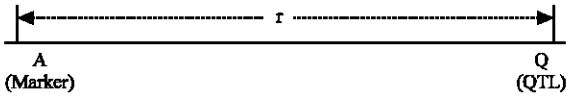
- This approach does not depict likely position of QTL. It can not thus distinguish between tight linkage to a QTL with small effect and loose linkage to a QTL with large effect.

The above disadvantages in two approaches were mostly because of the fact that only one marker is analyzed at one time. It is based on comparison of marker genotype means by:

- A simple t-test
- An analysis of variance
- A linear regression
- A likelihood ratio and maximum likelihood estimation

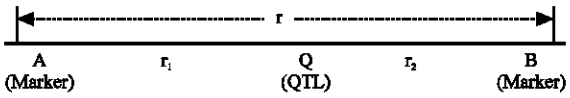
The QTL is determined to be located near a marker, if phenotypic values for the trait are significantly different among marker genotypes. The basic assumptions in single marker analysis approach are:

- Genes can be mapped on genome like simple genetic markers
- Genetic markers are linker with genes controlling quantitative traits.
- Genes and markers cosegregate due to linkage relationship.



r = Recombination frequency between A and Q

Interval mapping of QTL detection: Single QTL-analysis methods suffer from low statistical power and confounding of QTL effects with locations. To overcome these shortcomings Lander and Botstein (1989) proposed interval mapping approach, which is based on linkage relationships between a QTL and flanking markers.



If A and B are markers flanking a QTL Q with recombination frequencies λ_1 (A↔Q) and r_2 (B↔Q), then the recombination relationship, in absence of interference, is;

$$r = r_1 + r_2 - 2\,r_1\,r_2$$

The components of interval mapping are:

Table 2: Expected frequencies of Marker-QTL genotypes in a BC population

Marker genotype	Observed count	Frequency	QQ	Qq
AA BB	n_1	0.5 (1-r)	0.5 (1-r)	0
AA Bb	n_2	0.5 r	0.5 r_2	0.5 r_1
Aa BB	n_3	0.5 r	0.5 r_1	0.5 r_2
Aa Bb	n_4	0.5 (1-r)	0	0.5 (1-r)

- Likelihood approach
- Regression approach
- Combination of likelihood and regression approach

The approach of interval mapping considers one QTL at a time. Using a conventional backcross progeny, the linkage relationships can be studied by analysis of joint segregation of markers and QTL. Such a model for two flanking markers A and B and a QTL Q can be represented as follows:

AAQQBB (P_1) x aa qq bb (P_2)

↓

Aa Qq Bb (F_1) x AA QQ BB (P_1)

			Expected frequency
Backcross progeny	AA QQ BB	Aa Qq Bb	0.5 (1- r)
	AA Qq Bb	Aa QQ BB	0.5 r_1
	AA QQ Bb	Aa Qq BB	0.5 r_2
	AA Qq BB	Aa QQ Bb	0

The expected frequencies of Marker-QTL genotypes in a backcross population assuming no double cross-overs presented in Table 2.

It is clear from Table 2 that in case of tight linkage between A and B, the absence of any double cross over can be well assumed and consequently the frequency of marker-QTL genotypes i.e., AA Qq Bb and Aa QQ Bb (which can result from double cross overs) can be treated as zero. The interval mapping procedure are only meant for cases where Marker-QTL order is AQB because if the order is either ABQ or QAB, the analysis is same as single-marker analysis.

The position of a QTL vis-a vis its flanking markers is given by the quantity ρ, such that $\rho = r_1/r$, if $\rho = r1/r = 0$, then the QTL is located right on marker A, if $\rho = 1$, the QTL is located on marker B and if $\rho = 0.5$, the QTL is located in the middle of genomic segment AQB.

Interval mapping is also done by likelihood approach which is based on co-segregation of QTL and two flanking markers. It is assumed that each of the marker-QTL class has equal variance and the trait values are normally distributed.

Assuming a QTL with genetic effect g = 0.5 (μ_1 and μ_2), where μ_1 and μ_2 are the trait values of homozygote QQ and the heterozygote Qq and the trait variances of QTL genotypes (QQ and Qq) are equal i.e., σ^2. The expected QTL genotypic frequencies with four marker genotypes are:

QTL	AABB	AABb	AaBB	AaBb
QQ	1	0.5	0.5	0
Qq	0	0.5	0.5	1

The regression approach of interval mapping uses data on marker genotypes, trait phenotype, linkage relationships between A, B and Q and the expected trait values of marker genotypes to detect the existence of a QTL 'Q' between A and B, asses its effects and work out the genomic position of the QTL.

Multiple interval mapping (composite interval mapping): The interval mapping approach considers one QTL at one time. However, in many cases multiple QTL's are located in a single linkage group (Kao *et al*., 1999). In order to account for such multiple QTL's Zeng (1994) proposed the idea of combining Interval mapping with multiple regression. MIM is based on Cockerhams model for interpreting genetic parameters and the maximum likelihood method for estimation of genetic parameters. MIM is an improvement over single QTL analysis (Sen and Churchil, 2001), with the ability to separate linked QTL on same chromosome and to detect interactions among these QTL's. It provides increased power of detecting QTL's and eliminating the bias in estimates of effect and location of QTL's. MIM approach also gives reliable estimates of epistasis between QTL, the genotypic values of individuals and heritabilities of the quantitative traits.

Assuming m QTL's Q_1, Q_2……, Q_m located at positions p1, p2….pm in m different marker interval I_1, I_2 …… I_m along the genome controlling trait y. The quantitative trait value for an individual I can be related t m putative QTL's by the model (Kao *et al*., 1999).

$$Y_i = \mu + \sum_{j-1} aj\ xij + \sum_{j\#k}^{m} \sigma_{jk} (w_{jk}\ x_{ij}\ x_{ik}) + e_{ij}$$

where,

μ = Mean,
x_{ij} = Coded variable of genotype Q_j,
σ_{jk} = Indicator of epistatsis between Q,
a_j = Main effect of Q_j,
w_{jk} = Epistatic effect between Q_j and Q_k and
E_{ij} = Error assumed to follow N (o, σ^2)

Multiple trait QTL mapping: All the approaches discussed so far aim at mapping QTL trait by trait. Knott and Haley (2000) proposed a multi-trait QTL mapping

approach for use with three generation out bred pedigrees. This approach provides the statistical framework for testing pleiotropy of a QTL or whether more than one linked QTL are segregating. Mangin *et al.* (1998) also proposed alternate procedures for multiple trait mapping using canonical transformation of original data.

Recently Wu *et al.* (1999) has used a multi-trait least square method to analyse the tiller number in rice. They used RIL's. The approach is similar to the one proposed by Knott and Haley (2000), which used multi variate regression based on analysis of an F_2 population from a cross of two inbred lines. The basic model of this approach is

$$Y = XB + E$$

Where,
Y is a matrix (n x t), where n is number of F_2 individuals and t is number of traits,
X is the design matrix (n x p), where p is the number of explanatory variables.
B is a matrix (p x t) containing values of all traits and
E is a matrix (n x t) containing error values for all traits.

Application of QTL mapping to rice: Rice has been a model plant for almost all genomic and molecular biology studies owing to unique features of its genome and more importantly, the fruits of such research are going to affect a major shift in food productivity and human nutrition because it feeds more than half of world population. Rice has the smallest and one of the most compact genomes among cereals. The mapping of rice genome for identification of gene segments governing the important agronomic traits began with the development of RFLP map by Mc Couch *et al.* (1988). Since the earlier works of Ahn *et al.* (1993) and Xu *et al.* (1993), the research on QTL's in rice has resulted in documentation of over 1000 QTL's till 2000. Xiao *et al.* (1996) used Back Cross (BC_2) generation of a cross between *O. sativa* and *O. rufipogon* and identified various markers on chromosome 1 and 2 which were linked to QTL's accounting for 18 and 17% yield increase, respectively. In fact rice is the first monocot in which a major gene has been cloned through map based cloning (Xa21, the bacterial blight resistance gene) by Song *et al.* (1995). Yano *et al.* (2000) identified a QTL for heading date (Hd1) by same approach. Table 3 shows some of the QTL's mapped for different traits using molecular markers in rice.

QTL analysis and role in rice breeding: The improvement of quantitative traits has been important goal for most rice breeding programmes. Conventional breeding programmes as applied in rice requires a large amount of land, labour and money. Therefore plant breeders are interested in identifying as early as possible, the lines which contain those QTL alleles that contribute a large value of trait under selection. The discovery of different classes of molecular markers and their association with such QTL's conditioning different traits has greatly facilitated this process. Mapping of markers linked to QTL's actually identifies the genomic regions that may contain genes involved in the expression of a quantitative trait. The statistical and molecular analysis of QT's provide powerful tools to plant breeders which not only act as selection tools but also as starting points for cloning of the genes.

Advances in molecular genetics have enabled detection of at least some of the genomic regions affecting quantitative traits. The knowledge of genotype of individuals for QTL, either did directly or through linked markers can thus greatly enhance the genetic improvement of quantitative traits (Dekkers and Settar, 2004).

QTL analysis has produced great advances in plant breeding. Various research areas of applied significance in rice breeding programmes are:-

Genetic analysis of complex traits: Some of the important traits of economic importance like yield, disease resistance etc are complex in inheritance and therefore difficult to evaluate. Hence the efficiency of phenotypic selection is quite low. The advent of different marker system allows assaying of all genomic regions for linkage of such markers with genomic regions containing genes governing such complex traits. The results of such assays helps in map based cloning of genes. Rice is the first monocot in which a gene Xa 21 (Song *et al.*, 1995) for resistance against blast was cloned.

Plant genomics: Rice is the model plant in genomic research and results of the structural, functional and comparative genomic studies are going to be key in our efforts to enhance productivity, quality and sustainability of our food production systems. The advances in genome mapping have made it possible to map the genomic regions containing loci controlling QT's as well as determine the magnitude of effect of such loci (Xu, 2002). This is followed by relating the genetic and physical maps. The target region is then sequenced to identify genes within that region. Since QT's are conditioned by genes with small effects with sizeable interactions with genetic background and environmental factors, the greatest challenge to rice geneticists is identification and quantification of such minor effect QTL's which often

Table 3: Potential QTL's mapped in rice using different mapping populations for various growth, physiological and yield traits

Trait	QTL	Marker	Population	Reference
Plant height	qPH1-1	RZ730-RZ801	IR64/Azucena DH	Lu *et al.* (1996)
	qPH-1-2	RZ776-RG375	9024/Moreberekan RIL	Xiao *et al.* (1996)
	qPH-1-3	RG612	Co39/Moroberekan RIL	Huang *et al.* (1996)
	qPH-2-1	RZ213	IR64/Azucena DH	Yan *et al.* (1999)
	qPH-3-1	RG418-RM148	IR64/ToG5981/IR64 BC	Lorieux *et al.* (2000)
	qPH-4-1	RG143-RG620	Tesanai 2/CB F2	Zhuang *et al.* (1997)
	qPH-5-1	RG182-RG-9	-do-	-do-
	qPH-6-1	RZ682-RG653	9024/LH422RIL/9024	Xiao *et al.* (1995)
	qPH-7-1	RG351	Co39/Moroberekan RIL	Huang *et al.* (1996)
	qPH-8-1	RG333-RZ562	9024/LH422RIL/9042	Xiao *et al.* (1995)
	qPH-9-1	RZ9106-RZ777	Lemont/Teqing RIL	Li *et al.* (1995)
	qPH-10-1	G1082-G291	Zhaiyeqing 8/Jingxi 17 DH	Lu *et al.* (1996)
	qPH-11-1	RG118	Tesanai 2/CB F3	Zhuang *et al.* (1997)
	qPH-12-1	RG869	CO39/Moroberekan RIL	Huang *et al.* (1996)
Heading date				
	qHD-1-a	RG472-RG246	IR64/Azucena DH	Li *et al.* (2003)
	1HD-2-a	RG 171-RG157	-do-	-do-
	QHD-3-a	RG104-RG 348	-do-	-do-
	QHD-4	RG908-RG90	-do-	-do-
	qHD-5-a	RG556-RZ556	-do-	-do-
	qHD-6	R3226	Nipponbare/Kasalath BC_4F_2	Yamamoto *et al.* (2000)
	qHD-6-a	RG213-Amp	IR64/Azucena DH	Li *et al.* (2003)
	qHD-7	C560	Nipponbare/Kasalath BC_4F_2	Yamamoto *et al.* (2000)
	qHD-8-a	RG978-RG1	IR64/Azucena DH	Li *et al.* (2003)
	qHD-9	RZ206-RZ422	-do-	-do-
	qHD-10	RZ447-RG241	-do-	-do-
	qHD-11	G44-RG247	-do-	-do-
	qHD-12	AF6-RG457	-do-	-do-
Grain weight				
	qGWT-1	RG374-RG394	Tesanai 2/CB F_2	Lin *et al.* (2000)
	qGWT-2	RG157-RG171	-do-	-do-
	qGWT-4	RG143-RG214	-do-	-do-
	qGWT-4-a	RG7880RG190	Waiyin 2/CB F_2	-do-
	qGWT-5	RG13-RG573	Tesanai 2/CB F_2	-do-
	qGWT-5-a	CDO82-RG360	Waiyin 2/CB	-do-
	Q GWT-8	RZ66-RG598	Tesanai 2/CB F_2	-do-
No. of panicles/plant				
	qNP-2	RG157-RG171	-do-	-do-
	qNP-2-a	RG324A-RG324B	Waiyin 2/CB F_2	-do-
	qNP-4	RG143-R214	Tesanai 2/CB F_2	-do-
	qNP-5	RG360-RG9	Waiyin 2/CB	-do-
	qNP-6	Waxy-RG213	-do-	-do-
No. of grains/plant				
	qNG-1	RG274-RG394	Tesanai 2/CB F_2	-do-
	qNG-2	RG 25-RG 157	-do-	-do-
	qNG-8	RG 978-RZ66	-do-	-do-
	qNG-12	RG341-RG 235	-do-	-do-
Spikelet fertility				
	qSF-1	RG374-RG394	-do-	-do-
	qSF-6	Waxy-RG213	Waiyin 2/CB F_2	-do-
	qSF-8	RZ562-RZ617	-do-	-do-
1000-grain weight				
	qTGWT-1	RG173-RG532	Tesanai 2/CB	-do-
	qTGWT-4	RG143-RG214	-do-	-do-
	qTGWT-5	RG182-RG13	-do-	-do-
Embryo size				
	qEML-1	XNpb393-01	Asominori/IR24 RIL	Dong *et al.* (2003)
	qEML-2	C132	-do-	-do-
	qEML-3	R1468B	-do-	-do-
	qEMW-2	R712	-do-	-do-
	qEMW-8	XNpb 41	-do-	-do-
	qEMW-10	C1361	-do-	-do-
Seedling salt tolerance				
	qSGEM-6	RZ395-RG213	IR64/Azucena	Prasad *et al.* (2000)
	qSRTL-6	RG162-RG653	-do-	-do-
	qSDM-5	RZ76-RZ225	-do-	-do-
	qSV-6	CD0544-Amy2A	-do-	-do-
Cold tolerance				
	qSCT-1	--	ZYQS/Jx17 DH	Qian *et al.* (2000)
	qSCT-2	--	-do-	-do-
	qSCT-4	--	-do-	-do-

Table 3: Continued

Trait	QTL	Marker	Population	Reference
Brown plant hopper resistance				
	qBPH-2	--	--	Su *et al.* (1995)
	qBPH-10	--	--	-do-
	qBPH-12	--	--	-do-
Green leaf hopper resistance				
	Q GRH-5	--	--	Fujita *et al.* (1995)
	Q GRH-6	--	--	-do-
Blast resistance				
	qBR-2	--	F_4	-do-
	qBR-4	--	-do-	
	qBR-9	--	-do-	
	qBR-12	--	-do-	
No. of tillers				
	qTN-3	RZ284-PRD10A	IR64/Azukena DH	Nagabhushana *et al.* (2004)
	qTN-6	RM225-RM253	-do-	-do-
	qTN-10	RM239-G1084	-do-	-do-
	qTN-1	G359-RG140	CT9993/IR62266 DH	-do-
	qTN-2	R2417-RM212	-do-	-do-
	qTN-3-1	RG409-RG224	-do-	-do-
	qTN-2	R26-C424	IR36/Genjah Wangkal	Yamagishu *et al.* (2004)
	qTN-5	RM440-RM3870	-do-	-do-
	qTN-6	RM217-RM2147	-do-	-do-
Root/shoot length ratio	qTN-8	RM264-R1963	-do-	-do-
	qR/SL-1	CDO345-RZ909	-do-	-do-
	q RSR-4	C820-C933	Zhanshan 97/minghui 63	-do-
	q RSR-11	RM224-Y6854L	-do-	-do-
Root dry weight				
	q RDW-4-1	ME6-10-RG 449	-do-	-do-
	q RDW-2	RM240-RM213	-do-	-do-
	q RDW-3	RZ403-R19	-do-	-do-
	q RDW-4	C820-C932	-do-	-do-
	q RDW-5	R830-R3166	-do-	-do-
	q RDW-10	RM228-C405a	-do-	-do-
	Q RDW-11	RG118-C794	-do-	-do-
Total root Number				
	qTRN-4-1	RZ565-EMP3_10	-do-	-do-
Grain yield				
	q YLD-1-1	RZ513-RZ613	O. rufipogon/Calapo BC_2 F_2	Martinez and Thome (2001)
	q YLD-3-1	RG 100	Bg 90-2/O. rufipogon BC_2 F_2	-do-
	q YLD-5-1	RM13	-do-	-do-
	q YLD-6-1	RM217	-do-	-do-
	q YLD-9-1	RM215	-do-	-do-
	q YLD-9-2	RM242	-do-	-do-
	q YLD-11-1	RZ537-RZ900	O. rufipogon/Calapo BC_2 F_2	-do-
	q YLD-12-1	RG901	Bg 90-2/O. rufipogon BC_2 F_2	-do-
	q YLD-12-2	G1112	-do-	-do-
Grain protein (%)				
	q PRO-1	RM226-RM297	IRGC 103544/Caiapo DH	
	q PRO-2	RM6-RM112	-do-	-do-
	q PRO-6	RM190-RM253	-do-	-do-
	q PRO-11	RM209-RM229	-do-	-do-
Grain length				
	q GL-3	RM251-RM338	-do-	-do-
	q GL-6	RM 162-RM30	-do-	-do-
Amylose (%)				
	q AMY-3	RM7-RM251	-do-	-do-
	q AMY-6	RM190-RM253	-do-	-do-
	q AMY-8	RM230-RM264	-do-	-do-
Maximum root length				
	q MRL-3	C316-C63	Zhenshan 97/Minghui 63 RIL	Xu *et al.* (2002)
	q MRL-5	R830-R3166	-do-	-do-
	q MRL-7	RM 234-R1789	-do-	-do-
	q MRL-10	C1633-C667	-do-	-do-
	q MRL-311	C794-RZ918	-do-	-do-
Shoot dry weight				
	q SDW-1	C2340-C86	-do-	-do-
	q SDW-2	RM240-RM213	-do-	-do-
	q SDW-3	RG393-C1087	-do-	-do-
	q SDW-5	R3166-RG360	-do-	-do-
	q SDW-10	RG 561-RM228	-do-	-do-
	q SDW-11	RG118-C794	-do-	-do-

go undetected using small populations. The current techniques only allow low resolution mapping of QTL's (Kearrey and Farquhar, 1998). The development of refined procedures for high resolution mapping of QTL's can overcome such limitations and pave way for application of QTL analysis of physiological and agronomic traits for drafting metabolic pathway by candidate gene analysis (regulatory functions of genes) and also unveiling connections between different such pathways (Pleiotropic QTL's).

Germplasm enhancement: The limited genetic diversity of crop plants renders them more vulnerable to disease and insect epidemics and jeopardizes the potential for sustained genetic improvement in the long term breeding programme (Asins, 2002). The plant breeding process which depends on the genetic diversity is itself threatening the genetic base by involving only a few elite cultivars for developing new varieties. A huge amount of crop breeding efforts aim at acquisition and preservation of germplasm (An estimated 2.5 million crop entries in 700 documented seed collections). The massive germplasm collections are a great source of genes of economic interest. The localization of molecular markers in close proximity of the putative QTL's can be used to efficiently search for useful genes.

Increasing selection efficiency: The efficiency of selection for quantitative traits is greatly conditioned by the very nature of QT's. Even though conventional phenotypic selection will be an important component of crop breeding, the advances in molecular biology can greatly increase the efficiency of process. Several areas of focus in rice breeding are:-

- Several traits like male sterility restoration, wide compatibility, heterosis, combining ability, out crossing ability etc need several generations for identification of desirable plants. MAS can help eliminate such progeny testing because desirable genotypes can be identified by DNA-marker analysis.
- Several traits in rice need controlled conditions for optimum expression of genes (Photoperiod, temperature sensitivity, disease/insect resistance, salinity and submergence tolerance etc.). Selection for such traits can only be efficient when appropriate stress conditions are artificially created to isolate desirable plants. However, the application of linked markers can help indirect selection for these traits because screening for such traits is usually laborious and not so easy.
- Several traits like physical and chemical characteristics of seed, tissue culturability are not phenotypically scorable as they are not visible and thus need cumbersome laboratory techniques to ascertain different parameters of trait expression. If suitable markers are identified in close proximity of genomic regions governing these traits, MAS can be used to select the genotpypes with desirable parameters by accurate measurement of traits at any growth stage.
- Several traits such as heterosis, yield, quality etc can only be scored only after the reproductive stage. Molecular markers linked with QTL's contributing to heterotic expression for yield and component traits or quality such as aroma can be efficiently used to scan the genome for their presence at an early stage.
- Several traits like multiple resistance against different races of pathogens or insect biotypes are difficult to screen due to near absence of phenotypic differences in plants containing different genes for resistance. This necessisates use of multiple races/ biotypes of pathogens/insects to identify desirable plants which is not practically feasible. Different markers linked to different genes conferring such trait can be used to analyse plants with-out resorting to actual screening. This is an important concept in gene pyramiding.

Studying gene expression across growth and development: Plant gene expression is variable along the growth and development process. Most of the QTL analyses have focused on trait values at specific growth stages which does not fully reveal the action of genes during the development of trait (Xu, 2002). Yan *et al.* (1998) studied tiller number and plant height in IR64/Azucena DH population by interval mapping by phenotyping at every 10 days after transplanting. They found that some QTL's that were detected in early growth stages were not detected later on. They also found that only a few of the identified QTL's had a continuous activity all along the growth stages and concluded that genes at different growth stages have differential levels of expression.

QTL analysis for comparative studies: It has been found, as a result of extensive studies on grasses, that there is a high level of similarity or conservation of gene order in grasses. Comparative studies have revealed a close correspondence among QTL's conditioning certain traits in different cereals like rice, maize, wheat, barley, sugarcane and barley. Rice genome offers unique

opportunities in this regard. Not only can the results be interpreted for it, but also applied to other crops where such genomic sturdiest are not as feasible as rice. Besides such results can be also applied to certain Orphan Crops, which don't warrant such expensive studies owing to their less economic worth. The presence of high synteny among cereals can help identify orthologous QTL's. Besides close correspondence of QTL's among different species may help interpret results obtained in model species like rice to other crops with greater reliability.

Limitation of QTL analysis: The predicted amount of success in QTL analysis has been hamphered by the following limitations (Liu, 1998).

- QTL's are hypothetical genes based on statistical inferences only. Thus genetic effects used in QTL mapping could have very little biological importance. Even statistically the QTL effects are highly influenced by linkage. The repulsion phase linkage lowers the peaks while as coupling phase leads to overestimation of QTL effects.
- Most of the times the genetic models on which QTL mapping is based are not accurate because quantitative traits are more complex than what are presumed. Based on such genetic models the estimated QTL effects may mean nothing because oversimplification of models leads to wrong conclusions.
- The low resolution of QTL mapping is biggest problem in cloning of QTL's (Map based cloning). This is especially true for species with large genomes. Low resolution in QTL analysis is due to:-
    - Too much confidence in QTL position.
    - Inadequate significance levels.
    - Over-simplified genetic models.
    - The information generated by QTL analysis may not be adequate.
    - The present set of statistical and computational package though highly refined are not powerful enough to deal with epistatic interactions between QTL's.

CONCLUSIONS

QTL's analysis is more than just a statistical inference. Even though breeding programmes in near future will have conventional methods as important components, nevertheless, Modern approaches of molecular genetics and biotechnology will hold the key to our progress. In fact it will need a compatible combination of both conventional and non-conventional methods which will determine the success of crop improvement programmes. In fact the traditional approaches of quantitative genetics will need a coherent integration with molecular genetics and genomics to address the burning issue of population explosion and rice being the important cereal for mankind will hold key in this regard. Such an integration of all available approaches will lead to better understanding of quantitative trait inheritance.

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