



## Quantitative Trait Loci (Qtl) in Livestock and Poultry: A Review

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### Abstract

QTL is a site present on the chromosome at which a gene or group of genes affecting a quantitative trait is located. Techniques like backcross and intercross are used to detect genetic markers. Variation in quantitative trait is correlated with these markers. Moreover, quantification of each locus can be done and amount of variation in the trait can be noted. Specific areas can be target using this information and this knowledge can be used in future for understanding the genome and QTL present in it. However, the genes should be identified in a particular region and their function should be known. Detailed genomic mapping should be done to fully utilized the ability of QTL identification. With the help of QTL mapping, we can detect the variation of a trait in a given population. Moreover, we can know how much environmental factors play role in variation of a trait. Different type of polymorphic genetic markers is used in QTL mapping and certain techniques involving these markers makes it easier for identification of QTL. This QTL technique will further help in increasing the trait of interest in a population and decreasing the undesirable traits in a population. In future it can help in increasing the trait and profit related to that trait.

**Keywords:** QTL; Traits; Chromosome; Gene; Markers

### Abbreviations

QTL: Quantitative Trait Loci; QTN: Quantitative Trait Nucleotide; PSE: Pale Soft and Exudative; GDF8: Growth Differentiation Factor 8; ANOVA: Analysis of Variance; DNA: Deoxyribonucleic Acid; F1: First Filial Generation; LOD: logarithm of Odds; CIM: Composite Interval Mapping; MLE: Maximum Likelihood Estimation; MAS: Marker-Assisted Selection; SNP: Single Nucleotide Polymorphisms; BTA: Bos Taurus Autosome; OPN: Osteopontin; RIR: Rhode Island Red

### Introduction

Livestock and Poultry are reared on the basis of the certain traits. These traits can be classified as qualitative traits and quan-

titative traits. Qualitative traits are under the control of few genes whereas quantitative traits are controlled by polygenes. There is low environmental influence on qualitative traits whereas quantitative traits are highly influenced by environment. Traits like coat colour, presence or absence of horns, ABO blood groups are examples of qualitative traits. Traits like disease resistance, production, growth rate and Height are examples of quantitative traits. Quantitative traits can easily be classified into distinct phenotypic classes whereas it is difficult to classify quantitative traits into distinct phenotypic classes. Moreover, it is seen that qualitative traits exhibit discontinuous variation and are represented by binomial distribution. On the other hand quantitative traits exhibits continuous variation and are represented by normal distribution.

Quantitative trait loci is a chromosomal site at which the gene or group of genes affecting a quantitative trait is located. Quantitative traits are also called polygenic traits [1] as they are under the control of several loci and several genes. Identification and mapping of these loci are done in several species which showed specific chromosomes responsible for different traits. The term QTL was first coined by Gelderman in 1975 [2].

### QTL characteristics

As these traits are controlled by polygene, they each segregates according to Mendel's law. Environmental factors exert a large effect on quantitative traits. Moreover, a trait is controlled by many genes and allelic variations are fully functional. There is small effect of individual gene and the genes involved can be dominant or co-dominant. The genes involved when they are subjected to epistasis or pleiotropic effect. Epistasis is a phenomena in genetics in which the effect of gene mutation is dependent on the presence or absence of mutation in one or more other genes [3]. Pleiotropic effect states that multiple trait is affected by single gene or in other words the gene controls more than one traits. For example, Halo-thane gene in pigs is responsible for PSE and also effects carcass composition in pig [4]. Another example is double muscling gene (mutation of GDF8 gene) causes hyper trophy in cattle along with its effect on protein content and fatty acid profile [5].

### Requirement of QTL

Classical Mendelian Genetics lacks the flexibility to study the genes individually. It is mainly due to loss of gene effect in statistical fog as there is no adequate knowledge about genes, show some unrealistic assumptions were made to understand the individual properties of these genes [6]. Major assumptions include that all the gene frequencies at all the locus are more or less the same but in reality these gene frequencies vary from animal to animal. Second assumptions was that gene effect is same in all the animals however, it is not true as gene effect changes with environmental conditions. Similarly, dominance relation also varies because QTL is influenced by number of genes [6]. Recently, certain methods have been developed to overcome these difficulties. These methods are known as QTL technique.

### Advantage of QTL over classical mendelian system

Identification of individual genes could lead to several useful applications. It could improve a efficacy of selective breeding spe-

cially for the traits with low heritability or traits measured in one sex. Transgenic technology can be applied to quantitative traits. Identification of alleles that cause common diseases like diabetes could lead to improvement in method of prevention. Moreover, QTL knowledge can be applied in field of Medicine to increase disease resistance trait among animals.

### Methods of QTL

#### Non- normal distribution

It is a distribution in which data can be clumped upon one side either left or right. Based on gene frequency it can be platykurtic, skewed and leptokurtic [7]. There is a detectable departure of a gene from normality if it does not produce an effect which is large enough to cause multimodal distribution [6]. In other words, we can say that non normal distribution produces multimodality.

#### Heterogeneity of variance

If there will be heterogeneity of variance within the family then segregation of major gene occurs. This test requires very large sample size to detect heterogeneity of variance. The major drawback of this test is factors other than segregating major genes can cause heterogenous within the family variance [8]. This method was used for detection of major genes affecting *Drosophila* abdominal bristle number in segregating population [9].

#### Offspring-parent resemblance

The offspring mean will resemble more closely to the mid parent value than the single parent value if there is polygenic inheritance and absence of major gene. The reverse will be true if there is segregation of a major gene. The term Structured exploratory data analysis was given to a different group of test by Karlin, Carmelli and Williams in 1979 [10]. In a population a family of mice known to be segregating for hg gene was studied using major gene index [11].

#### Complex segregation analysis

It was mainly developed for study of human pedigree of parents and full sibs. It is considered as one of the most appropriate approaches for detection of major genes affecting quantitative variation in Complex segregation analysis [8]. Complex segregation analysis also provides evidence that whether the phenotypic trait is inherited in Mendelian dominant, co-dominant or recessive manner [6]. It also provides information that distribution of a

given phenotypic trait is under the effect of major gene or not. The purpose of Complex segregation analysis is to provide the initial evidence that a particular trait is affected by single gene and for this we only need phenotypic information, no genotypic information is required.

### QTL mapping

It is define as the process of constructing linkage maps and conducting QTL analysis [12]. In other words it is a technique to identify genomic regions associated with traits. The basic requirements for mapping QTLs are covering whole genome using a linkage map of polymorphic marker loci and the second requirement is that the quantitative trait should vary within or between population or strains.

### Objectives of QTL mapping

The major objectives of QTL mapping are mainly identification of genomic region that is affecting a trait of interest. The effect of QTL on the trait is analyzed. The amount of variation caused by a specific region in a trait is calculated. The effect of gene is also known that is either it is additive or dominant. The major objective of QTL mapping is to know the association between a trait of interest and the favorable allele.

### Principles of QTL mapping

Principle of QTL mapping includes to see the similarities between chromosomal segment from parents to offspring. In other words, to understand that chromosomal segment differ with respect to quantitative trait in individuals that inherit alternative chromosomal segment. The information about animals and genotype at marker locus provides the knowledge of chromosomal region which is getting transmitted [13]. If a QTL is located in a chromosomal region the more accurate estimate of breeding value can be done. Moreover, all the other QTLs affecting a trait can be known and their additive gene effects can also be studied.

### Steps of QTL mapping

The initial step in mapping any QTL is developing a mapping population in which the study has to be performed. Once the selection of mapping population is done a linkage map is generated. Then mapping population is subjected to phenotyping i.e. phenotypic traits are studied. Once all this knowledge is collected certain statistical tools like ANOVA, Maximum likelihood estimation etc are used for detection of our desired QTL.

### Methods of mapping QTL

There are various methods for QTL mapping which includes marker loci, QTL genotype, Single marker analysis, Interval mapping, Multiple test, Maximum likelihood estimation and Multiple QTLs.

### Marker loci

Marker loci is defined as a locus on a chromosome that can be identified using different method like Restriction fragment Length polymorphism, Randomly amplified polymorphic DNA and Variable number of tandem repeats. This helps in linkage analysis and isolation of a gene. The ideal marker loci show the following characteristics; highly polymorphic i.e. it should show some degree of variability in population, abundant i.e. it should cover the whole genome, neutral i.e. it should equal to both with the respect to all the QTL of interest and reproductive fitness, co dominant i.e. all the possible genotypes at the marker loci can be identified [14].

### QTL genotypes

Basically two different methods have been designed for identification and mapping of QTL in which lines that differ for trait of interest are crossed [6]. The other one is based on segregating population. For an effective experimental design certain lines are fixed for alternate alleles at both QTL and marker loci and there crossing is done. This is mainly done as there is maximum linkage disequilibrium between the loci in F1 generation. One parent line should be homozygous that is alleles which increase the value of a trait. Similarly, fixation of alleles that decrease the value of trait in other parent line should be done.

### Single marker analysis

Association between molecular marker and trait of interest can be detected using one of the series of quantitative trait loci analysis. It is also known as single point analysis. It is the simplest method for detection of QTL with single marker [15]. Only basic statistical software programme is required. There is no need of complete linkage map. The statistical methods that are used include T-Test, ANOVA and linear regression out of which linear regression is most commonly used. As the distance between marker and QTL increases the chances of detection of QTL decreases. Another disadvantage is it cannot determine that whether marker is associated with one or more marker QTLs. As QTLs are cofounded with recombinant frequencies their effect is underestimated [16].

### Interval mapping

Two markers are analysed at one time in interval mapping. It is considered as extension of individual marker analysis and interval between a QTL position. An interval within a QTL position can be determined using two markers. Further interval mapping is of four types namely, simple interval mapping, composite interval mapping, multiple interval mapping and Bayesian interval mapping [17].

### Simple interval mapping

Designated as SIM. Two markers are placed adjacent to a suspected area in which QTLs can be present on both sides. LOD score/curve is used to know the position of QTL [17]. The peak of an LOD score is considered to have a QTL for target trait. When the LOD score crosses a three value it is considered as evidence for linkage. Less than -2 LOD score is considered to exclude the linkage. The calculation of LOD score is done by dividing probability of birth sequence with given linkage by probability of birth sequence with no linkage. The advantage of simple interval mapping is it is more powerful than single marker analysis. A localization of the QTL on the linkage map is provided by LOD score curve. The representation of QTL position is done by support interval. The precision is high as they are not confounded.

### Composite interval mapping

Designated as CIM. For each analysis a few additional single markers are incorporated in composite interval mapping. In composite interval mapping we can obtain the information about number and position of QTLs and QTL interaction [17]. The advantage of composite interval mapping is it has very high level of precision and there is improvement in resolution of QTL location.

### Multiple tests

Most of the time the basic assumption is made that QTL is linked to a single marker or a pair of markers. However, if we see the practical view markers are distributed throughout the genome and testing of each marker is done for the linkage through QTL. Tests for linkage to the marker have to be repeated for each trait as multiple traits could be present in a parent line. Due to these chances of positive association are there. To overcome this, level of significance must be set stricter [6].

### Maximum likelihood estimation

Also known as MLE. The correct distribution properties of marker genotypes with respect to segregating QTL are considered. This makes maximum likelihood estimation and appropriate method for parameter estimation and significance test [18]. Observed data and parameters to be estimated are specific in likelihood estimation. The observed data is calculated as number of individuals and their phenotypes in each marker class and parameters are calculated as recombinant fraction, mean and variance of QTL groups. To calculate the likelihood function unknown parameters are selected and trial values are assigned, and iterative computer programme is used. Those trial values that maximize the likelihood function are considered as MLE of unknown parameter.

### Multiple QTLs

The parent line that differ at many loci affecting the trait of interest are choosed for mapping. Usually, the QTLs that are unlinked to markers are ignored by the scientists however, segregation of this QTLs in F2 or backcross generation are often seen [6]. So due to segregation of unlinked QTLs variance within the marker genotype classes occur. Moreover, these are effective factors rather than loci with which QTL identification by linkage to marker loci is done. So, effect observed when a QTL is linked to a marker is not due to one loci but due to two or more loci. This is an aggregated effect of two or more loci. The alleles may be in association or dispersion at linked loci. If they are in association the effect of separate loci may be smaller and if they are in dispersion the effect may be larger.

### Application of QTL

We can apply QTL in various ways such as it can be used to find genes/ markers that can be implemented in breeding programme via MAS. It allows the researchers to find the link between certain phenotypes and specific regions of chromosomes [19]. There is a demand of traits that affects behavior, production and wellbeing of the animal. These traits can be increased using QTL mapping. The development of molecular markers to locate QTL provides opportunity for incorporating MAS as a tool for increasing the efficacy of genetic improvement. In field of medical science QTL analysis has been proved to overcome certain genetic diseases.

### Genetical and statistical consideration

Certain genetical and statistical considerations are made to overcome the issue related with declining sample size, number and density of marker.

- As QTL effects are cofounded, we usually prefer interval

mapping over single marker analysis. Moreover, interval mapping is way more effective than single marker analysis.

- It is seen that backcross design is less effective than F2 design. The reasonable explanation to this can be that in backcross to a single parent only heterozygous effect is detected whereas both homozygous and heterozygous effects are detected in F2 design. Therefore, in backcross design we need four times more individual that were needed in F2 design [6].
- There is increase in a sample size to achieve the power level of fixed marker alleles in case of two parent population that are fix for alternative alleles, but marker alleles are segregating.
- It is seen that the power to detect difference in mean between two marker genotypes is independent of absolute value of the difference [6]. However, its dependence on within marker class standard deviation is seen. So, to increase the power of a test we can imply the strategies that reduce the standard deviation. More accurate estimation or accurate estimation of phenotypic values can reduce standard deviation.

### Future perspective of QTL

Emergence of a powerful tool like genome wide association study has define novel genes and made it easier to study molecular pathways involved in susceptibility or resistance to various disease [20]. With modernization there is significant development in genetic science that could improve both quality and quantity of QTL in future genotype-phenotype studies. As DNA screening is getting easier it provides enormous volume of genetic data to discover novel types of QTL. It helps us to better understand of the phenotypic and genotypic relationship and utilized a discovery of QTLs in medicine and production. Certain undesirable traits can be eliminated by this method in upcoming future generations. It helps us to understand more effectively and clearly how a phenotype is linked to genotype.

### Quantitative trait nucleotide (QTN)

In livestock many QTLs affecting economic traits have been identified. Between individuals of same species genetic variation occurs which mainly includes large chromosomal rearrangements and small insertion, deletion as well as single nucleotide polymorphisms. When this single nucleotide polymorphism is statistically linked to phenotype it becomes QTN. Two QTNs in namely DGAT1 and ABCG2 were detected in dairy cattle [21]. The advantages of

QTN over QTL are determination of confidence interval of individual QTL by linkage an analysis spans tens of map units, which contain 100 of genes. However, linkage disequilibrium reduced confidence interval but still it will contain tens of genes so, it is better to identify QTN than QTL. The polymorphism that is responsible for observed variation of QTL is called QTN. The utility of QTN includes that after identification of QTN if both of the alleles are segregating the frequency of favorable allele within a breed can be enhanced [22]. Interrogation of allele into the breeds can be done even if the allele is absent. This increases the frequency of favorable allele.

### QTL database

Data can be divided into genes centric and trait centric views using specific tool in QTL database. As data is organized in a particular manner it makes easier for the users to follow the information flow. Users can search their queries using gene name, symbol and any other known names. Moreover, the detailed information of each gene and number of QTLs that are associated with that gene are also indicated. The database was originally developed to house pig QTL in 2005. Recently in 2020 Goat is added to animal QTL database. In Cattle, a total of 1,61,781 QTLs were identified representing 680 different traits. Related to these 1,049 publications are present in QTL database [23]. Similarly in Chicken, a total of 14,058 QTLs related to 438 different traits are identified. A total of 350 publication related to these QTLs are present in animal database [23].

### QTLs reported in cattle

QTL affecting milk production traits in water buffalo are reported. There has been identification of four SNP in two genomic region that were associated with milk production trait in water buffalo. First region was affecting milk fat and protein percentage and was located on BTA3. Similarly, the other region affecting total milk yield, fat yield and protein yield was located on BTA14 [24].

Single Marker Analysis and Interval Mapping techniques were employed for identification of QTLs related with milk yield in Murrah buffalo. A total of 63 QTLs were identified by Single Marker Analysis and 32 QTLs were identified by Interval mapping. A total of 23 chromosomal regions were identified for milk yield in Murrah buffalo. Two meta-QTL chromosomal regions were identified on buffalo chromosome BBU2q, three meta-QTLs on each buffalo chromosomes BBU8, 10 and 15 were identified. Four meta-QTL re-

gion each on BBU1q, BBU6 and BBU9 were identified [25].

In Holstein Friesian cattle QTL related to lameness associated phenotypes are reported on chromosome no. 3 where three genomic regions were identified. Moreover, QTL associated with digital dermatitis and interdigital hyperplasia was present. On chromosome no. 23 QTL associated with interdigital hyperplasia was identified and on chromosome no. 2 QTL associated with sole haemorrhage was identified [26].

Five novel QTLs that are associated with resistance to Bovine Tuberculosis were reported to be present on BTA13 [27].

The effect of osteopontin gene variants on milk production traits in Holstein Friesian crossbred cattle of Kerala was studied and it was reported that OPN gene was located on bovine chromosome no. 6. Moreover, two alleles were found namely T allele and C allele and it was concluded that there was significant difference in milk production between CT and TT genotypes animal. Moreover TT genotypes showed more milk production [28].

#### QTLs reported in sheep

In Sheep candidate genomic regions for body weight and some major gene effects were found to be present on chromosome no. 1, 2, 3, 4, 5, 6, 16, 18 and 20. [29].

The presence of QTL on OAR5 and OAR25 and one QTL in ovine chromosome 20 was reported. A total of 22 associations were identified resulting in quantitative trait loci influencing somatic cell score in Sheep [30].

In Sheep QTLs were associated with growth and meat traits are also reported with a total of 156 SNPs associated traits and 165 gene associated with growth and meat traits was found in different breeds of sheep [31].

A total of 261 candidate genes associated with morphological and agronomic traits of wild and domestic sheep were reported [32].

Three QTLs were associated with expression of quantitative trait loci in Sheep liver and muscle that contribute to variation in meat traits. A total of three QTLs were reported within each tissue. Moreover, identified QTLs were associated with 56 carcass traits

and fatty acid profiles [33].

#### QTLs reported in goat

In Goats chromosomal regions associated with milk production traits were found at 59 centimorgan in CHI3. These QTLs were related to milk production traits in Goat [34].

A total of 109 genes were associated with dairy traits (milk production traits) in goat and chromosome 14 contain a major region that was associated with fat content [35].

In Tropical Indian Goat breed the two microsatellite loci were reported to be associated with mean faecal count and packed cell volume as traits in population with *Haemonchus contortus* infection [36].

Twelve candidate genes were reported that played important role in regulation of litter size and ovarian development in goats [37].

Even QTL related to Mohair traits in Irani Angora goats are reported and they were found to be present on chromosome 1, 2, 5, 13, 19 and 24 [38].

#### QTLs reported in swine

A total of 339 expression quantitative trait loci were mapped in pigs. Analysis of these QTLs when linked to phenotypic QTLs revealed that 16 genes were associated with meat quality, carcass composition and growth traits [39].

Genomic wide association study revealed that a total of 88 genes were related to disease resistance in Chinese Jiangquhai breed of pig [40].

Presence of 23 miRNA expression QTLs in pig longissimus dorsi muscle was reported. Moreover one expression quantitative trait loci was found to be related with 12 production traits including back fat thickness, dressing percentage, muscle pH at 24 hour post-mortem and cook yield [41].

Three genes namely EIF3M, DNAJC24 and ARL14EP were found to be present on 1.6 Mb region on SSC2 is found to be associated with antibody response to classical swine fever vaccination. [42].

Three genotypes were reported in Mizo local pig population

by using PCR-RFLP technique. Moreover, the association of porcine growth hormone gene with growth performance in hill pig of Mizoram was reported [43].

### QTLs reported in poultry

Influence of sire microsatellite genotypes on prehousing body weights and mortality was reported in RIR chickens. Moreover, the influence of sire and hatch on early layer economic traits was also reported [44].

There was significant influence of microsatellite genotypes on age at sexual maturity in RIR chickens. Finding suggested that faster genetic progress was seen in RIR flocks by adapting microsatellite-based genotype selection [45].

A total of 30 QTLs were detected by half sib analysis and seven QTLs were detected by full sib analysis that were associated with fatty acid composition in Korean native chicken. Out of 30 QTLs 12 were present in thigh region and 18 were present in breast region and out of seven QTLs three were present in thigh region and four were present in breast region [46].

There was identification of five genomic regions in different chromosomes in which QTL for morphometric and mineral composition trait of the tibia bone in broiler and layer cross were reported [47].

Identification and validation of QTL for ascites syndrome in broiler chicken was done using whole genomic sequencing which result in identification of 28 regions [48].

### Conclusion

Two types of information (genotypic and phenotypic data) are linked using the statistical method known as QTL. Certain genetic markers made our research easier in field of QTL detection. Further, many QTLs affecting economic traits in livestock and poultry has been identified. These QTLs can be implemented to increase production in a livestock. In cattle QTL for most common and important traits (milk production and disease resistance) has been identified and studied. Identification of QTL related to fat percentage in pigs is done. Egg production and body weight QTLs are main focused in poultry, similarly in sheep QTL related to meat traits and carcass weight and QTLs related to litter size and disease resis-

tance in goats has been identified and studied. Hence, identification of QTL related to particular trait provide us the opportunity to increase the desired trait. Further it benefits the farmers as high yielding animals can provide great profit to the farmers.

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