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Understanding Gene Interaction Through Genomic and System Biology for Crop Improvement

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Epistasis is considered as an important genetic phenomenon as it plays vital but untapped role in trait development in crop. In classical mendelian genetics, epistasis is reflected as departure from expected Mendelian segregation ratios (Morre, 2003). While, any statistical interaction that involves two or more loci is referred to as epistasis in quantitative genetics. Which is reflected by the modification of additive and/or dominance effect. When epistasis occurs, the effect of one locus is genotype-dependent for the associated loci. Characteristics of quantitative traits are consequence of gene interaction networks and parameters that control the dynamics of networks. Understanding gene interaction networks will advance our knowledge of genetic basis of the quantitative variation of several economic traits. Unravelling the interactions between loci can help predict how agricultural crop species will respond to artificial selection and how inbreeding would affect their performance.

In natural populations, buried quantitative genetic variation is caused by epistasis. The QTL effect size estimates are biased when the experiment is not performed using population with wide genetic base ideally possessing all possible alleles of the interacting loci. Employing information about interaction effects mediated by certain alleles at other genomic locations may enhance the improvement achieved by introgression of such identified gene/QTL. Genomics facilitates the reconstruction of gene network. The direction of biology is shifting from the classical biology through molecular biology to system biology (Friedman and Perriman, 2007). In era of system biology, quantitative genetics makes a paradigm shift towards systems quantitative genetics. It employs dynamic network model which depicts real biological features of quantitative traits (Zhu et al., 2009). Ways to study gene interaction can be listed under three levels: 1) Interaction between mutations, 2) QTL-QTL interaction and 3). Network study or system biology.

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Interaction between mutations:

Large-scale genetic interaction screening is made possible by the collection of deletion mutants and high throughput techniques for producing and identifying double mutants. A series of query mutations and a target mutation were used to study interactions in yeast. (St Onge et al.,2007). Small world networks and guilt-by- association principle allows features of network topology to be inferred. With these principles, interacting partners can be identified. An alternate approach is to carry out genome-wide investigations to determine how single and double mutants differ from controls in terms of gene expression. Genes showing differential expression patterns could be considered as a candidate gene controlling the trait.

QTL-QTL interactions:

Several traits of interest in the field of agriculture (biological) and medical sciences often under the control of multiple interacting factors. Identification of the interacting loci may facilitate the exploration of the architecture of quantitative traits (Hanlon et al., 2006). When polymorphic alleles are present in a mapping population with a frequency of 0.5, the ability to detect QTL interactions is at its highest (Mackay, 2014). Interaction effects between QTLs can be as significant as main effects and could occur between QTLs which are not significant when considered alone (Mackay, 2014). For example, two QTLs that regulate the differences between the plant and inflorescence architecture of teosinte and maize interact epistatically (Doelby, j. et al.,1995). Two novel epistatic QTLs, which are epistatically interacting QTLs that alter growth rate, are revealed in Arabidopsis NILs for an area with no overall effect (Kroyman et al.,2005).

System biology:

large scale molecular measurements and computational modelling are the key element of system biology. No gene is more or less important than other. System biologists sees a larger and holistic picture than in reductionist approach. Under system biology, epistasis is the functional interaction between gene partners with respect to trait development (including hierarchical or non-hierarchical relationships. In addition, system biology incorporates both continuous expression pattern of genes i.e. molecular quantitative genetics and classical quantitative genetics to generate systems diagrams and genetic pathways. System biology employs a dynamic network model rather than a static model (Zhu et al. 2009).

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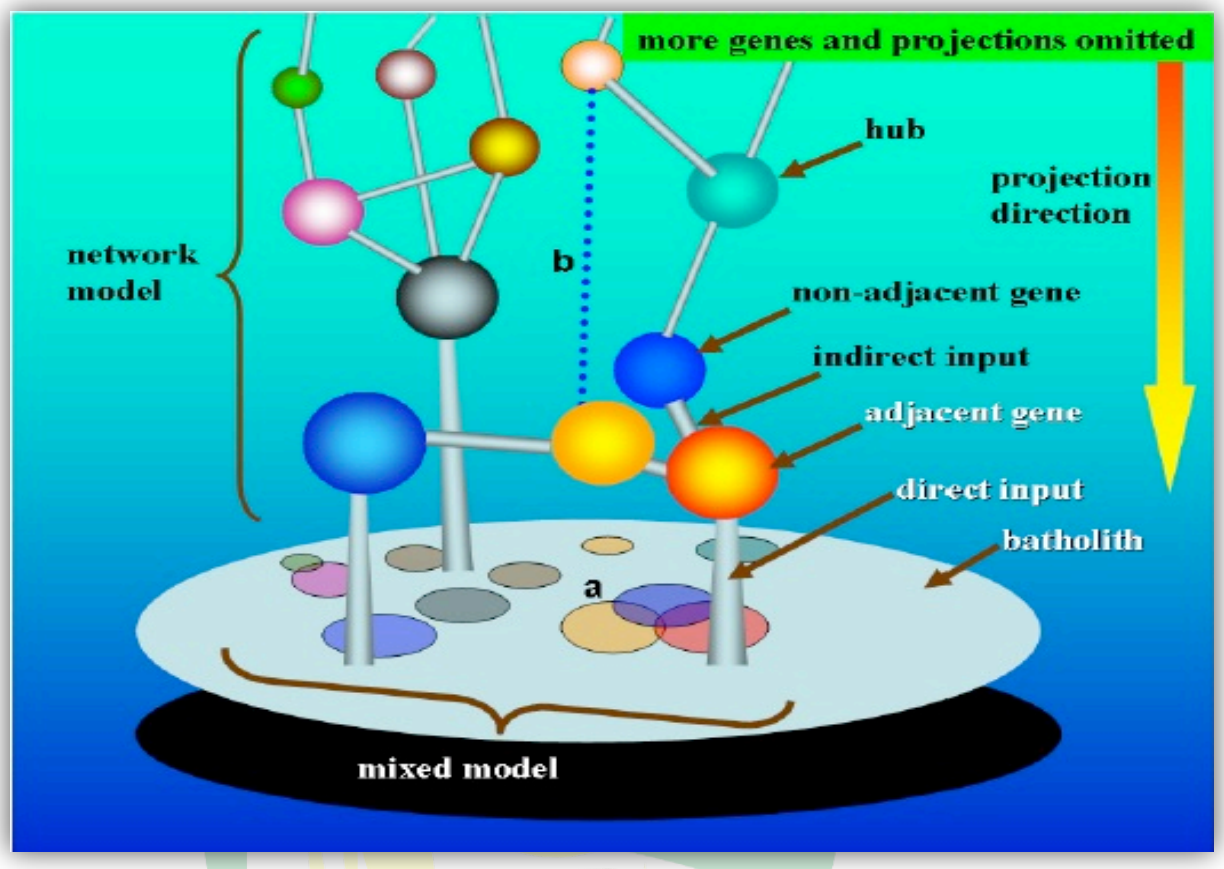

Fig.1 Hypothetical representation of quantitative genetics and interaction of genes under network model (Figure adopted from Zhu et al., 2009)

The working model is illustrated in Fig. 1. a) Mixed model: The size of the projected area denote effect size of gens in the system and the overlapped area depicts the interaction level (2 points interaction, 3 points interaction and son on). While in b) network model: The genes interact through the regulatory links in development dependent manner. The effect on the batholiths receives the direct information only from adjacent gene while the effect of non-adjacent gene is indirect and through interaction with the adjacent gene. The regulatory genes are developmental stage specific and mixed model is dynamic rather than static. It is imperative that system biology models can be used to established genetic relationships and genomic systems diagrams.

Drawbacks and challenges:

- Microarray profile cannot be established for every mutation.

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- Exploring higher order interaction requires large population with multiple phenotypic measurements.
- Confounding effect of knocked out upstream gene with gene having null effect on the trait of interest.
- It is difficult to assign a biologically appropriate scale for widely variable expression values among genes.
- Designs for detecting novel epistatic patterns is complicated and not cost-effective without large-scale heliotype data.

Conclusion:

The of filed biology have advance from classical to molecular era. Recently biology is making a paradigm shift to system biology. The complex genetic nature of quantitative traits, polygenic variation, and high environmental influence often makes their utilization in crop improvement difficult. The quantitative variation is often hidden and differentiating their effects in analyses from main effects is difficult. Interaction term should not be ignored while describing the genetic architecture of complex traits. Studying the interaction among genes/QTL is a tool to understand genetics of quantitative traits better. Heritability of QTls can be studied in wider dimensions and trait improvement will be more efficient. Recently, phenotypic data generated using microarray techniques is handy for constructing genetic networks on a genome scale. Although systems biology makes its entrance, with its arrival of system biology the reductionist approach might become outdated.

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