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Genetics and population analysis

QTLNetwork: mapping and visualizing genetic architecture of complex traits in experimental populations

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ABSTRACT

Summary: QTLNetwork is a software package for mapping and visualizing the genetic architecture underlying complex traits for experimental populations derived from a cross between two inbred lines. It can simultaneously map quantitative trait loci (QTL) with individual effects, epistasis and QTL–environment interaction. Currently, it is able to handle data from F_2, backcross, recombinant inbred lines and double-haploid populations, as well as populations from specific mating designs (immortalized F_2 and BC_nF_n populations). The Windows version of QTLNetwork was developed with a graphical user interface. Alternatively, the command-line versions have the facility to be run in other prevalent operating systems, such as Linux, Unix and MacOS.

Availability: http://ibi.zju.edu.cn/software/qtlnetwork

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1 INTRODUCTION

Mapping quantitative trait loci (QTL) for complex traits has become a routine tool in functional genomic research. With the advent of highly dense genetic maps of various organisms, a large number of systemic statistical approaches and the corresponding software have been established to dissect the phenotypic variation into several genomic regions, which greatly facilitated the downstream candidate genes discovery and cloning. Most of the prevalent QTL mapping software such as MapMaker/QTL (Lander *et al*., 1987), Map Manager (Manly *et al*., 2001), QTL Express (Seaton *et al*., 2002), R/qtl (Broman *et al*., 2003) and WinQTLCart (Wang *et al*., 2006) were developed and implemented interval mapping (Haley and Knott, 1992; Lander and Botstein, 1989), composite interval mapping (Zeng, 1994) or multiple-interval mapping (Kao *et al*., 1999). However, none of these tools can simultaneously investigate epistasis and QTL–environment (QE) interactions. In the present study, we developed a new QTL mapping software called 'QTLNetwork' to dissect the genetic architecture of complex traits into single-locus effects (additive and/or dominance), epistatic effects (additive by additive, additive by dominance, dominance by additive and dominance by dominance) and their QE interaction effects, and also to visualize the analysis results by a series of graphs.

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2 METHOD AND DEVELOPMENT

QTLNetwork was developed based on a novel QTL mapping method that has been published in this journal (Yang *et al*., 2007). The method begins with marker interval analysis to select candidate marker intervals that might to be linked with QTL(s). These selected marker intervals are subsequently used as cofactors in a 1D genome scan for putative QTL (Fig. 1a). Secondly, the analysis of marker–interval interaction is conducted to detect significant marker–interval interactions. After that, a 2D genome scan procedure is performed to search for epistasis conditioned on the previously detected QTL and marker–interval interactions (Fig. 1b). All these analyses are implemented in a mixed linear model framework with Henderson method III (Searle, 1992) to construct the *F*-statistic, and with a permutation test (Doerge and Churchill, 1996) to calculate the critical *F*-value to control the genome-wise type I error. Finally, all the detected QTL and epistasis are fitted by a full-QTL model to estimate the main effect of QTL and epistasis and their interaction effects with environment by MCMC (Markov Chain Monte Carlo) algorithm (Wang *et al*., 1994), and to predict the genetic architecture of complex traits (Fig. 1c).

The computational code of QTLNetwork was written in standard C++ language, and thus can be complied in any operating system, such as Windows, Linux, Unix and MacOS. The GUI (graphical user interface) of QTLNetwork was developed in Microsoft Visual Studio with MFC (Microsoft foundation class) and the graphic visualizations were implemented by VTK (visualization toolkit). We also developed a web-service system of QTLNetwork based on Java and JSP (JavaServer Pages). Users can submit their data files to our Linux server via the URL, http://ibi.zju.edu.cn/-software/qtlnetwork/webservise/for remote analysis. After completing the analysis, the system will send the result file back to the users by email. Users can open the result files (with data files) with

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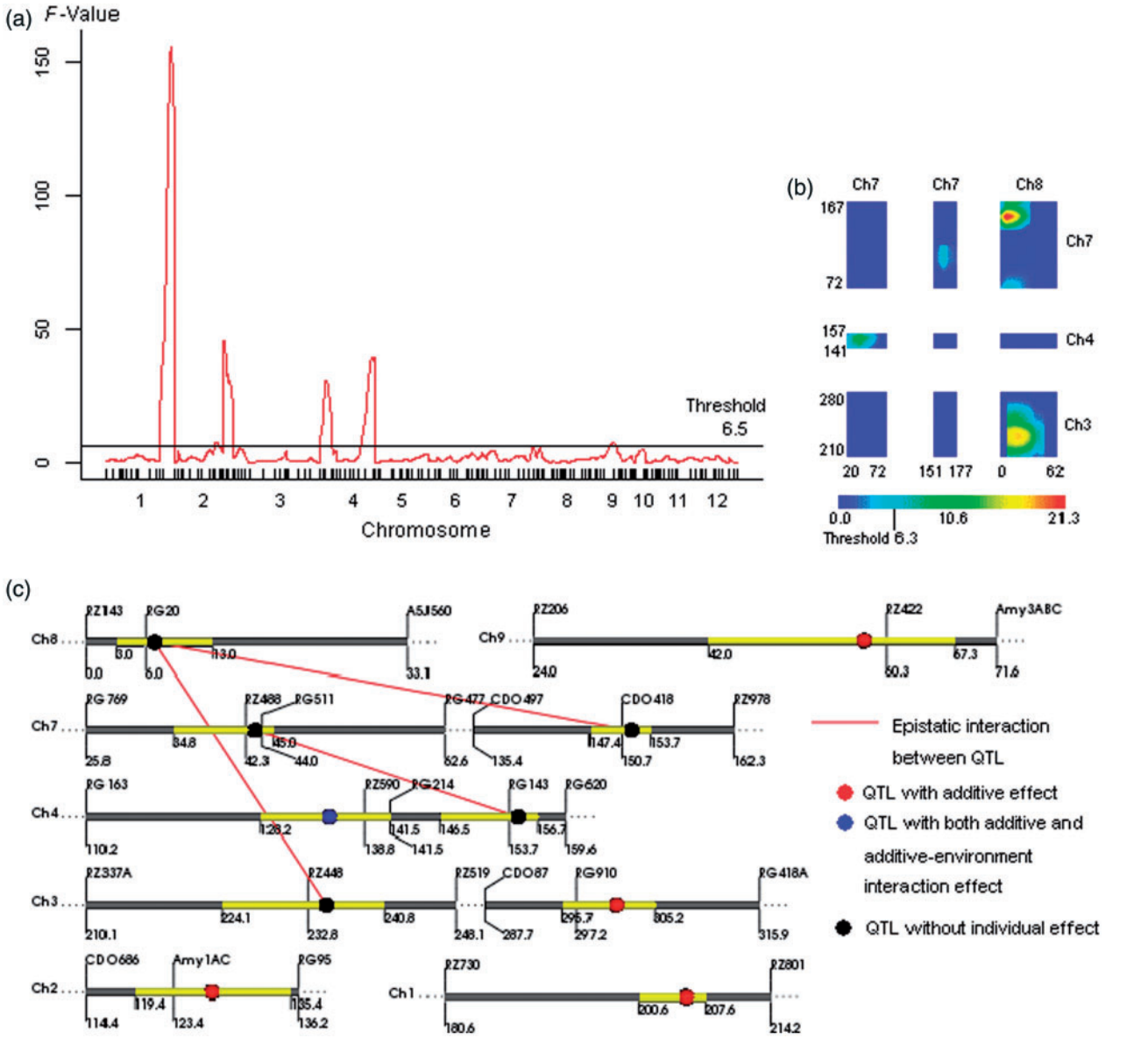

Fig. 1. Example graphs of QTLNetwork for plant height in rice. (**a**) *F*-statistic curve generated by a 1D genome scan. (**b**) *F*-statistic profile obtained by a 2D genome scan. (**c**) The predicted genetic architecture of plant height in rice (the chromosome regions in yellow represent the support intervals for QTL).

the GUI version of QTLNetwork on local machine to visualize the result.

3 CONCLUSIONS

QTLNetwork not only provide new QTL mapping approaches, but also facilitate the analysis results with a visualization environment, which can help the geneticists and breeders to better understand genetic architecture of complex traits. The software can handle data from various kinds of experimental populations derived from a cross of two inbred lines. Detailed information about the data analysis of QTLNetwork is available in the user manual.

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