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ORIGINAL PAPER

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Methods for predicting superior genotypes under multiple environments based on QTL effects

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Abstract Methods were developed for predicting two kinds of superior genotypes (superior line and superior hybrid) based on quantative trait locus (QTL) effects including epistatic and QTL × environment interaction effects. Formulae were derived for predicting the total genetic effect of any individual with known QTLs genotype derived from the mapping population in a specific environment. Two algorithms, enumeration algorithm and stepwise tuning algorithm, were used to select the best multi-locus combination of all the putative QTLs. Grain weight per plant (GW) in rice was analyzed as a working example to demonstrate the proposed methods. Results showed that the predicted superior lines and superior hybrids had great superiorities over the F_1 hybrid, indicating large breeding potential remained for further improvement on GW. Results also showed that epistatic effects and their interaction with environments largely contributed to the superiorities of the predicted superior lines and superior hybrids. User-friendly software, QTLNetwork, version 1.0, was developed based on the methods in the present paper.

Introduction

The advent molecular marker technique has greatly facilitated genetic analysis of quantitative traits. A number of statistical methods have been developed for mapping quantitative trait loci (QTLs). Based on maximum likelihood algorithm, Lander and Botstein (1989) proposed a systematical way to scan the genome for evidence of QTLs [interval mapping (IM)]. Zeng (1993, 1994) proposed the composite interval mapping (CIM) method to detect individual QTLs × conditioning the test on other selected markers. Jansen (1993, 1994) proposed a similar method to CIM and named it “multiple QTL model” or “marker–QTL marker” (MQM). Compared with IM, both CIM and MQM can significantly improve the mapping precision.

However, the genetic architecture of complex trait consists of not only the actions of genes in singular locus, but also the inter-locus interactions and gene × environment interactions. More and more evidence indicating that the complexity of the genetic architecture can be largely attributed to epistasis has been provided, which plays a significant role in heterosis, inbreeding depression, adaptation, reproductive isolation, and speciation. Evolution researches have established that the assembly and maintenance of favorable epistatic combination adapted for a specific environment is a major mechanism of adaptation in various plant species (Allard 1996). In addition, the property that QTL effects are environmentally sensitive results in phenotypic plasticity or the ability of organisms to take on alternative developmental fates, depending on environmental cues (Lukens and Doebley 1999). With strong epistasis and genotype × environment interactions for fitness traits, local adaptation can be readily achieved (Li et al. 2001).

Realizing the importance of epistasis and QTL × environment (QE) interaction, some methods have been developed for analyzing QTLs with either epistatic effects (Fijneman et al. 1996; Kao et al. 1999; Zeng et al. 1999; Jannink and Jansen 2001) or QE interaction effects (Jansen et al. 1995; Jiang and Zeng 1995; Piepho 2000). A mixed-model-based composite interval mapping method (MCIM) has been developed for mapping QTLs with additive effects and epistasis effects of additive × additive, as well as their interaction with environments, by software QTLMapper, version 1.0 (Zhu 1999; Wang et al. 1999). Recently, Y.M. Gao and J. Zhu (submitted) extended the additive and additive × additive model by adding dominance effects, epistatic effects of additive ×

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dominance and dominance × dominance as well as their interaction with environments, and updated the software QTLMapper to version 2.0.

The genetic information obtained from QTL mapping experiments can be utilized in genetic improvement of the interested traits. In the present study, we derived general formulae for predicting the total genetic effect of individuals with known QTL genotypes in a specific environment. Moreover, we proposed methods for predicting two kinds of superior genotypes (superior line and superior hybrid) derived from the mapping population. Data on grain weight per plant (GW) collected from an immortalized F_2 (IF_2) population of rice were analyzed as a working example.

Materials and methods

In a specific environment, total genetic effect (G) consists of genetic main effect (G_G) and genotype × environment interaction effect (G_{GE}). Consider a population derived from a cross between two inbred strains (P_1 and P_2): the total G of P_1, P_2, and F_1, in the hth environment can be expressed as

$$\begin{aligned} G_h(P_1) &= G_{\mathrm{G}}(P_1) + G_{\mathrm{GE}_h}(P_1) \\ &= \left(\sum_i^n a_i + \sum_i^{n-1}\sum_{j=i+1}^n aa_{ij}\right) \\ &\quad + \left(\sum_i^n ae_{ih} + \sum_i^{n-1}\sum_{j=i+1}^n aae_{ijh}\right), \end{aligned} \tag{1}$$

$$\begin{aligned} G_h(P_2) &= G_{\mathrm{G}}(P_2) + G_{\mathrm{GE}_h}(P_2) \\ &= \left(-\sum_i^n a_i + \sum_i^{n-1}\sum_{j=i+1}^n aa_{ij}\right) \\ &\quad + \left(-\sum_i^n ae_{ih} + \sum_i^{n-1}\sum_{j=i+1}^n aae_{ijh}\right), \end{aligned} \tag{2}$$

$$\begin{aligned} G_h(F_1) &= G_{\mathrm{G}}(F_1) + G_{\mathrm{GE}_h}(F_1) \\ &= \left(\sum_i^n d_i + \sum_i^{n-1}\sum_{j=i+1}^n dd_{ij}\right) \\ &\quad + \left(\sum_i^n de_{ih} + \sum_i^{n-1}\sum_{j=i+1}^n dde_{ijh}\right), \end{aligned} \tag{3}$$

where n denotes the total number of QTLs, a_i is the additive effect of the ith QTL (Q_i); d_i is the dominance effect in heterozygote of Q_i; aa_{ij} and dd_{ij} are the digenic epistatic effects of additive × additive and dominance × dominance between Q_i and Q_j; ae_{ih} is the additive × environment interaction effect for Q_i; de_{ih} is the dominance × environment interaction effect for Q_i; aae_{ijh} and dde_{ijh} are the interaction effects between aa_{ij}, dd_{ij} and the hth environment, respectively.

For any pure line derived from this population, there are two possible genotypes (QQ and qq) at each locus. Thus, there are 2^n possible pure lines, and the total G of the kth pure line can be written as

$$\begin{aligned} G_h(L_k) &= G_{G_h}(L_k) + G_{GE_h}(L_k) \\ &= \left(\sum_i^n x_{ih(L_k)} a_i + \sum_i^n \sum_{j=i+1}^n x_{ih(L_k)} x_{jh(L_k)} aa_{ij}\right) \\ &\quad + \left(\sum_i^n x_{ih(L_k)} ae_{ih} + \sum_i^n \sum_{j=i+1}^n x_{ih(L_k)} x_{jh(L_k)} aae_{ijh}\right) \end{aligned} \tag{4}$$

where $x_{ih(L_k)}$ and $x_{jh(L_k)}$ refer the genotypes of the Q_i and Q_j of the kth line in the hth environment ($x_{ih(L_k)} = 1$ for Q_iQ_i , and $x_{ih(L_k)} = -1$ for q_iq_i), respectively.

If we intend to obtain a pure line with superior genotype in the hth environment, a direct way is to calculate the total G of all the possible lines and choose the most favorable one. However, the computing time of this enumeration algorithm grows exponentially with the number of QTLs. When the QTL number is larger than 27, this algorithm becomes very time-consuming. Therefore, we developed another algorithm (stepwise tuning algorithm, or ST algorithm) to deal with the case of large number of QTLs (see "Appendix"). Though the ST algorithm cannot guarantee a global optimal result, its computing complexity can be reduced from $O(2^n)$ to $O(n)$.

Furthermore, for any hybrid derived from the studied population, there are three possible genotypes (QQ, Qq, and qq) at each locus. Accordingly, there are $3^n - 2^n$ possible hybrids, and the total G of kth of these possible hybrids in the hth environment can be expressed as

$$\begin{aligned} G_h(H_k) &= G_{G_h}(H_k) + G_{GE_h}(H_k) \\ &= \{\sum_i^n x_{ih(H_k)} a_i + \sum_i^n (1 - |x_{ih(H_k)}|) d_i \\ &\quad + \sum_i^n \sum_{j=i+1}^n x_{ih(H_k)} x_{jh(H_k)} aa_{ij} \\ &\quad + \sum_i^n \sum_{j=i+1}^n x_{ih(H_k)} (1 - |x_{jh(H_k)}|) ad_{ij} \\ &\quad + \sum_i^n \sum_{j=i+1}^n (1 - |x_{ih(H_k)}|) x_{jh(H_k)} da_{ij} \\ &\quad + \sum_i^n \sum_{j=i+1}^n (1 - |x_{ih(H_k)}|)(1 - |x_{jh(H_k)}|) dd_{ij}\} \\ &\quad + \{\sum_i^n x_{ih(H_k)} ae_{ih} + \sum_i^n (1 - |x_{ih(H_k)}|) de_{ih} \\ &\quad + \sum_i^n \sum_{j=i+1}^n x_{ih(H_k)} x_{jh(H_k)} aae_{ijh} \\ &\quad + \sum_i^n \sum_{j=i+1}^n x_{ih(H_k)} (1 - |x_{jh(H_k)}|) ade_{ijh} \\ &\quad + \sum_i^n \sum_{j=i+1}^n (1 - |x_{ih(H_k)}|) x_{jh(H_k)} dae_{ijh} \\ &\quad + \sum_i^n \sum_{j=i+1}^n (1 - |x_{ih(H_k)}|)(1 - |x_{jh(H_k)}|) dde_{ijh}\}, \end{aligned} \tag{5}$$

where $x_{ih(H_k)}$ and $x_{jh(H_k)}$ refer the genotypes of the Q_i and Q_j of the *k*th possible hybrid in the *h*th environment ($x_{ih(H_k)}=1$ for $Q_\mathrm{i}Q_\mathrm{i}$, $x_{ih(H_k)}=0$ for $Q_\mathrm{i}q_\mathrm{i}$ and $x_{ih(H_k)}=-1$ for $q_\mathrm{i}q_\mathrm{i}$), respectively; ad_{ij} and da_{ij} are the digenic epitatic effects of additive × dominance and dominance × additive between Q_i and Q_j; ade_{ijh} and dae_{ijh} are interaction effects between ad_{ij}, da_{ij}, and the *h*th environment, respectively.

Similarly, we can get an environmental-specific superior hybrid with the enumeration algorithm. Because there are three possible genotypes per QTL, it is much more time-consuming than it is in predicting the superior line. When the QTL number is larger than 17, the computing time will sharply grow to be an astonishing number. Thus, it is recommended to use the ST algorithm to predict the superior hybrid with more than 17 QTLs.

Because genes may have different actions in different environments, the predicted superior genotypes will have different multi-locus combinations in different environments. Generally, the superior genotype predicted in one environment could not be applied in different environments where there existed large QTL × environment interactions. Hence, it is very necessary to predict environmental-independent superior genotypes based only on QTL main effects:

$$G_G(L_k)=\sum_i^n x_{i(L_k)}a_i+\sum_i^n\sum_{j=i+1}^n x_{i(L_k)}x_{j(L_k)}aa_{ij}, \tag{6}$$

$$\begin{aligned}G_G(H_k)=&\sum_i^n x_{i(H_k)}a_i+\sum_i^n\left(1-\left|x_{i(H_k)}\right|\right)d_i\\&+\sum_i^n\sum_{j=i+1}^n x_{i(H_k)}x_{j(H_k)}aa_{ij}\\&+\sum_i^n\sum_{j=i+1}^n x_{i(H_k)}\left(1-\left|x_{j(H_k)}\right|\right)ad_{ij}\\&+\sum_i^n\sum_{j=i+1}^n\left(1-\left|x_{i(H_k)}\right|\right)x_{j(H_k)}da_{ij}\\&+\sum_i^n\sum_{j=i+1}^n\left(1-\left|x_{i(H_k)}\right|\right)\left(1-\left|x_{j(H_k)}\right|\right)dd_{ij},\end{aligned} \tag{7}$$

where $x_{i(L_k)}$(or $x_{i(H_k)}$) and $x_{j(L_k)}$(or $x_{j(H_k)}$) refer the genotypes of Q_i and Q_j of the *k*th line (or hybrid).

In practice, the superior genotypes can be predicted based on the unbiased estimation of QTL main effects and unbiased prediction of QE interaction effects obtained in QTL mapping experiment.

Working example

As a demonstration of the methods proposed in the present paper, we analyzed the data of grain weight per plant (grams) collected from an immortalized F_2 population of rice, which were constructed with 240 F_1 hybrids obtained from randomly mating among the recombinant inbred lines (RILs) (Hua et al, 2002). These RILs derived from the cross 'Zhengshan 97B' × 'Minghui 63'' were provided by Prof. Qifa Zhang of Huazhong Agricultural University, Wuhan, China. There were 241 individual lines in the RIL population with a genetic linkage map consisting of 221 markers, covering 1,796.58 cM of the rice genome. The materials were evaluated in 1999 and 2000 at the experimental station of Zhejiang University, Hangzhou, China. The climate condition showed great variance in the 2 years.

Using QTLMapper, version 2.0, Y.M. Gao and J. Zhu (submitted) analyzed the marker genotype data and trait phenotypic observations; a total number of 25 QTLs as well as 15 digenic epistatic interactions were identified at a 0.005 significant level. The QTLs were

Fig. 1 Quantative trait loci network map on grain weight per plant of rice

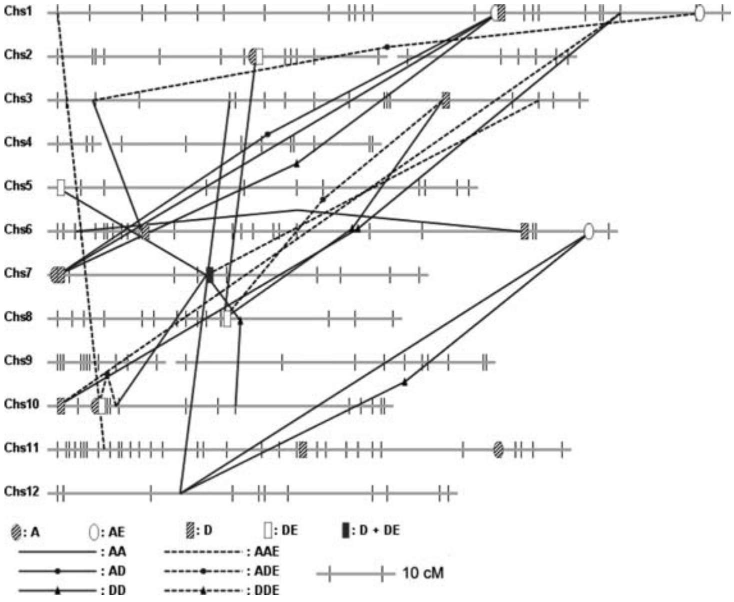

Table 1 Predicted (or estimated) genetic effects (*G*) for P_1, P_2, and F_1—superior line (*SL*) and superior hybrid (*SH*)—on grain weight per plant of rice. G_G General genetic effect, $G_1 = G_G + G_{GE_1}$ and $G_2 = G_G + G_{GE_2}$ are the total genetic effects in 1999 and 2000, respectively

Entry	G_G	G_1	G_2
P_1	−7.15	−7.26	−7.03
P_2	−2.70	−3.62	−1.77
SL	17.70	22.11	24.48
F_1	−0.47	0.62	−1.56
SH	18.7	23.66	20.43

The estimated population mean is 26.50; the threshold probability for significant QTL effects is 0.005

named as "Gw" along with the chromosomal number. If there were more than one QTL in a chromosome, the serial number was added after the chromosomal number. The whole genetic architecture information identified in the present study could be summarized to an informative QTL network map with the effect magnitudes being ignored (Fig. 1).

Utilizing the estimated QTL main effects (*a*, *d*, *aa*, *ad*, and *dd*), we predicted the general superior line (GSL) and general superior hybrid (GSH) as well as calculated the general genetic effects of them. We also predicted the superior lines (SLs) and superior hybrids (SHs) for different environments and calculated the corresponding total genetic effects based on their QTL effects. Because it was almost impossible to use the enumeration algorithm to predict SHs with 25 QTLs, we used the ST algorithm instead. In addition, we calculated the total genetic effects of P_1, P_2, and F_1 in the two environments. (All these results are presented in Table 1.) It was shown that the predicted total genetic effects of F_1 ('Shanyou 63') were higher than that of better parent in the 2 years, which was in consistence with the fact that 'Shaiyou 63' showed heterosis over better parent on GW. In 1999 and 2000, the predicted total genetic effects of SLs were much higher than that of F_1 in the corresponding year. In 1999, the predicted total genetic effect of SH was slightly higher than that of SL, but the reverse was true in 2000. In addition, the general genetic effect of GSL was a little lower than that of GSH, and both of them much higher than the general genetic effect of 'Shanyou 63'.

The QTL genotypes of the predicted GSL, SLs, GSH and SHs are listed in Table 2. It was shown that the QTL genotype of the predicted SL in 1999 differed from that in 2000 at four loci. Both of the predicted SLs in 1999 and 2000 could be obtained by substituting alleles between P_1 and P_2 at eight loci, respectively. The QTL genotype of predicted SH in 1999 differed from that in 2000 at six loci. If we want to obtain the predicted SHs in 1999 and 2000, we need to improve at least 11 and 10 QTLs, respectively. Nearly a half of QTLs of the predicted GSH and of the predicted SHs in 1999 and 2000 were homozygous, which might imply that additive effects and additive × additive epistatic effects as well as their QE interaction effects could be the major components to the superiorities of GSH and SHs.

Table 2 Quantative trait loci (*QTL*) genotypes (*QG*) of the predicted general superior lines (*GSL*s), SLs, general superior hybrids (*GSH*s), and SHs on grain weight per plant of rice

GSL		SL			GSH		SHs		
QTL	QG	QTL	QG		QTL	QG	QTL	QG	
			1999	2000				1999	2000
Gw1–14	*QQ*	Gw1–1	*QQ*	*qq*	Gw 1–14	*Qq*	Gw 1–1	*QQ*	*qq*
Gw 2–8	*QQ*	Gw 1–14	*QQ*	*QQ*	Gw 1–21	*Qq*	Gw 1–14	*Qq*	*Qq*
Gw 4–2	*qq*	Gw 1–21	*qq*	*QQ*	Gw 2–8	*qq*	Gw 1–21	*Qq*	*Qq*
Gw 4–5	*qq*	Gw 1–22	*QQ*	*qq*	Gw 4–2	*qq*	Gw 1–22	*QQ*	*qq*
Gw 7–1	*qq*	Gw 2–8	*QQ*	*QQ*	Gw 4–13	*Qq*	Gw 2–8	*qq*	*Qq*
Gw 8–3	*qq*	Gw 4–2	*qq*	*qq*	Gw 8–3	*qq*	Gw 4–2	*qq*	*qq*
Gw 8–15	*QQ*	Gw 4–5	*qq*	*qq*	Gw 8–15	*QQ*	Gw 4–13	*Qq*	*Qq*
Gw 8–26	*QQ*	Gw 4–15	*qq*	*QQ*	Gw 8–26	*QQ*	Gw 7–1	*QQ*/*qq*	*Qq*
Gw 8–28	*QQ*	Gw 7–1	*qq*	*qq*	Gw 8–28	*Qq*	Gw 8–3	*qq*	*qq*
Gw 9–1	*QQ*	Gw 8–3	*qq*	*qq*	Gw 9–1	*Qq*	Gw 8–15	*QQ*	*QQ*
Gw 9–4	*QQ*	Gw 8–15	*QQ*	*QQ*	Gw 9–4	*Qq*	Gw 8–26	*QQ*	*QQ*
Gw 10–12	*QQ*	Gw 8–26	*QQ*	*QQ*	Gw 10–12	*Qq*	Gw 8–28	*Qq*	*Qq*
Gw 13–2	*QQ*	Gw 8–28	*QQ*	*QQ*	Gw 13–1	*Qq*	Gw 9–1	*Qq*	*Qq*
Gw 13–5	*qq*	Gw 9–1	*QQ*	*QQ*	Gw 13–2	*QQ*	Gw 9–4	*Qq*	*Qq*
Gw 14–31	*qq*	Gw 9–4	*QQ*	*QQ*	Gw 14–31	*qq*	Gw 10–12	*Qq*	*Qq*
Gw 15–3	*QQ*	Gw 10–12	*QQ*	*QQ*	Gw 15–3	*Qq*	Gw 13–1	*Qq*	*Qq*
		Gw 13–1	*QQ*	*QQ*			Gw 13–2	*Qq*	*QQ*
		Gw 13–2	*QQ*	*QQ*			Gw 13–5	*qq*	*QQ*/*qq*
		Gw 13–5	*qq*	*qq*			Gw 14–9	*QQ*	*QQ*
		Gw 14–9	*QQ*	*QQ*			Gw 14–31	*qq*	*qq*
		Gw 14–31	*qq*	*qq*			Gw 15–3	*Qq*	*Qq*
		Gw 15–3	*QQ*	*QQ*					

Discussion

Impact of QTL mapping on the superior genotype predictions

Because superior genotype prediction is based on the results of QTL mapping, the reliability of the predicted superior genotype is directly affected by the precision of QTL mapping:

1. Both biased estimation of QTL main effects and biased prediction of QE interaction effects are deleterious to superior genotype prediction. Therefore, if the QTL mapping is conducted by a method that may cause biased estimation for QTL main effects and biased prediction for QE interaction effects, the predicted superior genotype will be unreliable.
2. The superior genotype predictions are very sensitive to the threshold probability chosen for QTL detection. With different significant levels, we could get different QTL mapping results, and consequently, get different superior genotype prediction results. The threshold probability should not be too low, otherwise the power of QTL detection would be dramatically reduced, and the predicted superior genotype will not be as superior as it should be. On the other hand, the threshold probability should not be too high, or else the predicted superior genotypes will be unbelievable. In QTL mapping practices, it is very difficult to determine a suitable threshold probability for declaring significant QTL effects. Sometimes, for different traits we might have to choose different threshold probabilities. Herein, we suggest that when the heritability of one trait is large enough, the estimated genotypic values of parents will be close to their observed values if an appropriate significant level is used in QTL mapping. In addition, we thought that it would be better to compare the different results of superior genotype predictions at different significant levels and select the most appropriate one by experience.

Implications for genetic breeding

Epistasis is an important genetic component underlying the variation of complex quantitative traits. The recently developed QTL mapping methods MCIM can simultaneously analyze epistasis and its interaction with environments (Zhu 1999; Wang et al. 1999; Y.M. Gao and J. Zhu, submitted). In the present study, digenic epistatic effects and their interaction with environments have been broadly detected for GW in rice (Fig. 1). Accordingly, the predicted superior genotypes will be unreliable if epistasis is ignored in QTL analysis. It has been revealed that the F_1 hybrid 'Shanyou 63' showed superiority over both parents, which was in good agreement with the fact that 'Shanyou 63' has been the best hybrid widely used in China for decades. We found that its superiority was mainly attributed to the *dd* and *dde* effects. For an instance, in 1999, the summed *d* and *de* effects contributed the predicted total genetic effect of F_1 negatively by −7.65, but the summed *dd* and *dde* effect contributed it positively by 17.19, indicating that *dd* and *dde* rather than dominance or overdominance were the major genetic components of heterosis for 'Shanyou 63' on GW. In addition, the estimated general genetic effects of GSL and GSH were both much higher than the estimated general genetic effect of 'Shanyou 63'. In 1999 and 2000, the predicted total genetic effects of SLs and SHs were also much higher than that of 'Shanyou 63'. It was concluded that there still existed potential for further increasing GW in breeding materials derived from 'Zhengshan 97B' × 'Minghui 63'. On the other hand, we found that although only four kinds of QTL effects (*a*, *aa*, *ae*, and *aae*) were utilized, the predicted SLs have already shown very high superiorities.

GE interaction is another important component of genetic basis. Understanding the genetic principle of *GE* interaction is of great importance to genetic breeding. In breeding practice, it is a risk to apply the superior genotype to various environments when it is predicted based on the QTL information obtained only in one environment. If the superior genotypes predicted in different environments are of great differences, their superiority may be dramatically reduced across environments. Hence, in order to develop broadly adaptable cultivars, we need to partition the QTL main effects and QE interaction effects, and conduct genetic improvement based only on QTLs with main effects. However, for a special environment, it is quite necessary to develop varieties specific for that environment by conducting QTL mapping study and genetic improvement on the traits of interest in that special environment.

Development of computer software

User-friendly windows software (QTLNetwork, version 1.0) was written in the C+ + language. This software is specially designed for the software QTLMapper and can only accept the data format generated by QTLMapper as input data. This software can be run on the operation systems of Microsoft Windows 9.x/2000/NT/XP. QTLNetwork 1.0 is freely available at http://ibi.zju.edu.cn/software/qtlnetwork/ and has the following features:

1. It can analyze the data of double haploid, RIL, F_2, and IF_2 populations.
2. It can present the QTL mapping results generated by QTLMapper in graphics and in text format.
3. It can predict SLs and SHs based on the results of QTL mapping.

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Appendix

Denote n as the total number of QTLs. The stepwise tuning algorithm can be described by the following procedure:

1. Initialize the genotype of an individual as the same genotype of P_1 and set $i = 1$.
2. To predict SLs, GSLs, SHs or GSHs, go to Procedure A, Procedure B, Procedure C, or Procedure D, respectively.
3. Set $i = i + 1$. If $i \leq n$ repeat step 2, otherwise, stop.

Procedure A

(1) If $i = 1$, calculate the total genetic effect of the individual in the hth environment $\left(\hat{G}'_h\right)$ using all the QTL effects.

(2) Change the genotype of the i-th QTL from Q_iQ_i to q_i q_i and calculate its total genetic effect $\left(\hat{G}'\right)$ again. If $\hat{G}'_h > \hat{G}_h$ (or $\hat{G}'_h < \hat{G}_h$), keep the change and set $\hat{G}_h = \hat{G}'_h$ otherwise, set the genotype of the ith QTL back to Q_iQ_i.

Procedure B

(1) If $i = 1$, calculate the general genetic effect of the individual $\left(\hat{G}_G\right)$ using only the estimated QTL main effects.

(2) Change the genotype of the ith QTL from Q_iQ_i to q_iq_i and calculate its general genetic effect $\left(\hat{G}'_G\right)$ again. If $\hat{G}'_G > \hat{G}_G$ (or $\hat{G}'_G < \hat{G}_G$), keep the change and set $\hat{G}_G = \hat{G}'_G$ otherwise, set the genotype of the ith QTL back to Q_iQ_i.

Procedure C

(1) If $i = 1$, calculate the total genetic effect of the individual in the hth environment $\left(\hat{G}_h\right)$ using all the QTL effects.

(2) Change the genotype of the ith QTL from Q_iQ_i to q_iq_i and calculate its total genetic effect of superior line $\left(\hat{G}'_h\right)$ again. If $\hat{G}'_h > \hat{G}_h$ (or $\hat{G}'_h < \hat{G}_h$), keep the change and set $\hat{G}_h = \hat{G}'_h$, otherwise, set the genotype of the ith QTL back to Q_iQ_i.

(3) Change the genotype of the ith QTL from Q_iQ_i to Q_i q_i and calculate its total genetic effect $\left(\hat{G}'_h\right)$ again. If $\hat{G}'_h > \hat{G}_h$ (*or* $\hat{G}'_h < \hat{G}_h$), keep the change and set $\hat{G}_h = \hat{G}'_h$, otherwise, set the genotype of the ith QTL back to Q_iQ_i.

Procedure D

(1) If $i = 1$, calculate the general genetic effect of the individual $\left(\hat{G}_G\right)$ using onlythe estimated QTL main effects.

(2) Change the genotype of the ith QTL from to q_iq_i and calculate its general genetic effect $\left(\hat{G}'_G\right)$ again. If $\hat{G}'_G > \hat{G}_G$ (or $\hat{G}'_G < \hat{G}_G$), keep the Q_iQ_i change and set $\hat{G}_G = \hat{G}'_G$, otherwise, set the genotype of the ith QTL back to Q_iQ_i.

(3) Change the genotype of the ith QTL from Q_iQ_i to Q_iq_i and calculate its general genetic effect $\left(\hat{G}'_G\right)$ again. If $\hat{G}'_G > \hat{G}_G$ (or $\hat{G}'_G < \hat{G}_G$), keep the change and set $\hat{G}_G = \hat{G}'_G$, otherwise, set the genotype of the ith QTL back to Q_i Q_i;

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