

Testing pleiotropy vs. separate QTL in multiparental populations

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Abstract

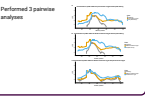
High-dimensional phenotypes in multiparental populations provide new opportunities for understanding complex trait architecture. New analysis tools are required. We developed a test of pleiotropy vs. separate QTL for multiparental populations. We applied it to bioinducers for separate QTL for behavioral phenotypes in a 2-cM region in Drosophila melanogaster. We share our methods in an R package, qtl2pleio (<https://github.com/Boehm/qtl2pleio>).

Test procedure

For the model:
$$Y = XB + G + E$$
for each ordered pair of markers:
$$G \sim MV(0, K, V_G)$$
$$E \sim MV(0, I, V_E)$$

- E contains allele probabilities
- G contains allele effects
- Calculate likelihood for each model fit
- Test statistic:
$$-2 \ln \left(\frac{\max_{\theta} L(\theta, Y, X, V)}{\max_{\theta} L(\theta, Y, X, V_0)} \right)$$
- Parametric bootstrap to get p-value

Profile LOD plots



3 pairwise tests

- Percent time in light* & "Test allele latency" $p = 0.108$
- "Distance traveled in light" & "Test allele latency" $p = 0.108$
- Percent time in light* & "Distance traveled in light" $p = 0.871$

Conclusions

- Evidence for two separate QTLs affecting the 3 phenotypes
- 1 QTL affects both "distance traveled in light" and "percent time in light"
- 2 separate QTLs containe Hydn and affects "Test allele latency"

Future directions

- Expression expression data from Keller et al. (2018)
- Expression QTL, linkage disequilibrium
- Statistical power studies

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References

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Introduction

Experimentalists can now measure tens of thousands of phenotypes with RNA sequencing and mass spectrometry. Multiparental populations enable high-resolution QTL mapping. Together, high-dimensional phenotypes and multiparental populations can inform complex trait genetics. New analysis tools, such as our test of pleiotropy vs. separate QTL, are needed.

Background

- Jiang and Zeng (1995) developed a pleiotropy vs. separate QTL test for two-parent crosses
- Applies to two tests that map two single genetic regions
- Pleiotropy in the null hypothesis
- Separate QTLs in the alternative hypothesis
- Perform a two-dimensional QTL scan
- Calculate likelihood ratio test statistic

Challenges in multiparental

- Redundance: Multivariate polynomic random effects
- Tight founder lines: if fixed effects
- Test statistic calibration: Parametric bootstrap test

Behavioral genetics

- Logan et al. (2013) and Reich et al. (2014) genotyped and phenotyped Drosophila melanogaster
- Identified Hydn as the chromosome 8 gene affecting "Test allele latency" at 51 cM
- Identified chromosome 8 QTLs for "percent time in light" and "distance traveled in light" at 51 cM
- Motivated us to ask if Hydn also affects "percent time in light" and "distance traveled in light"

Allele effects plots

- Support that "percent time in light" and "distance traveled in light" share a single QTL
- Hydn is distinct from that QTL