

Testing pleiotropy in multiparental populations

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Introduction

- 10,000+ traits with RNA sequencing and mass spectrometry
- Multiparental populations offer high-resolution QTL mapping
- New analysis tools, such as a pleiotropy test for multiparental populations, are needed

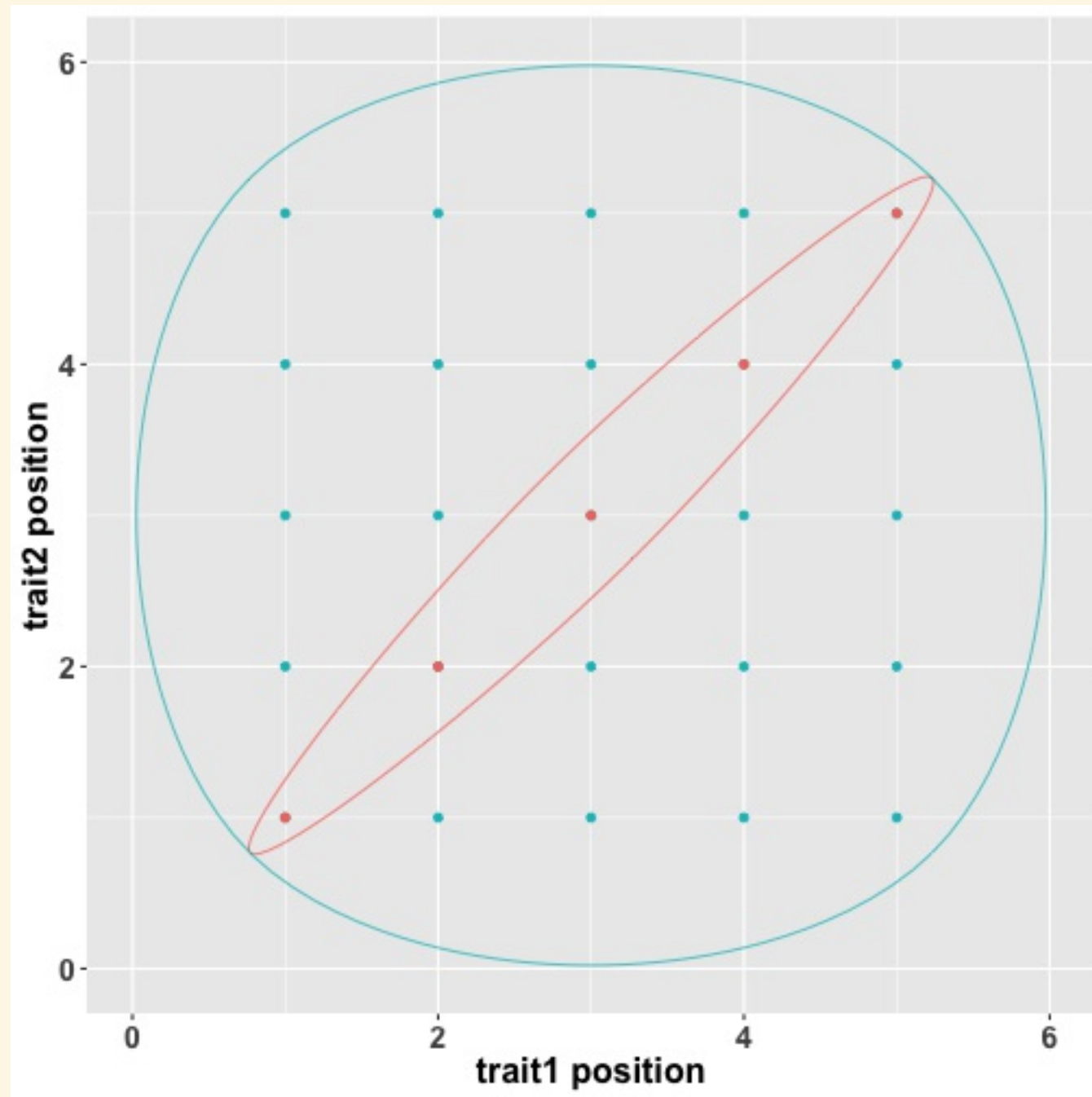
Jiang and Zeng (1995) test

- Two-parent crosses
- Applies to two traits that co-map
- H_0 : Pleiotropy
- H_A : Two separate QTL

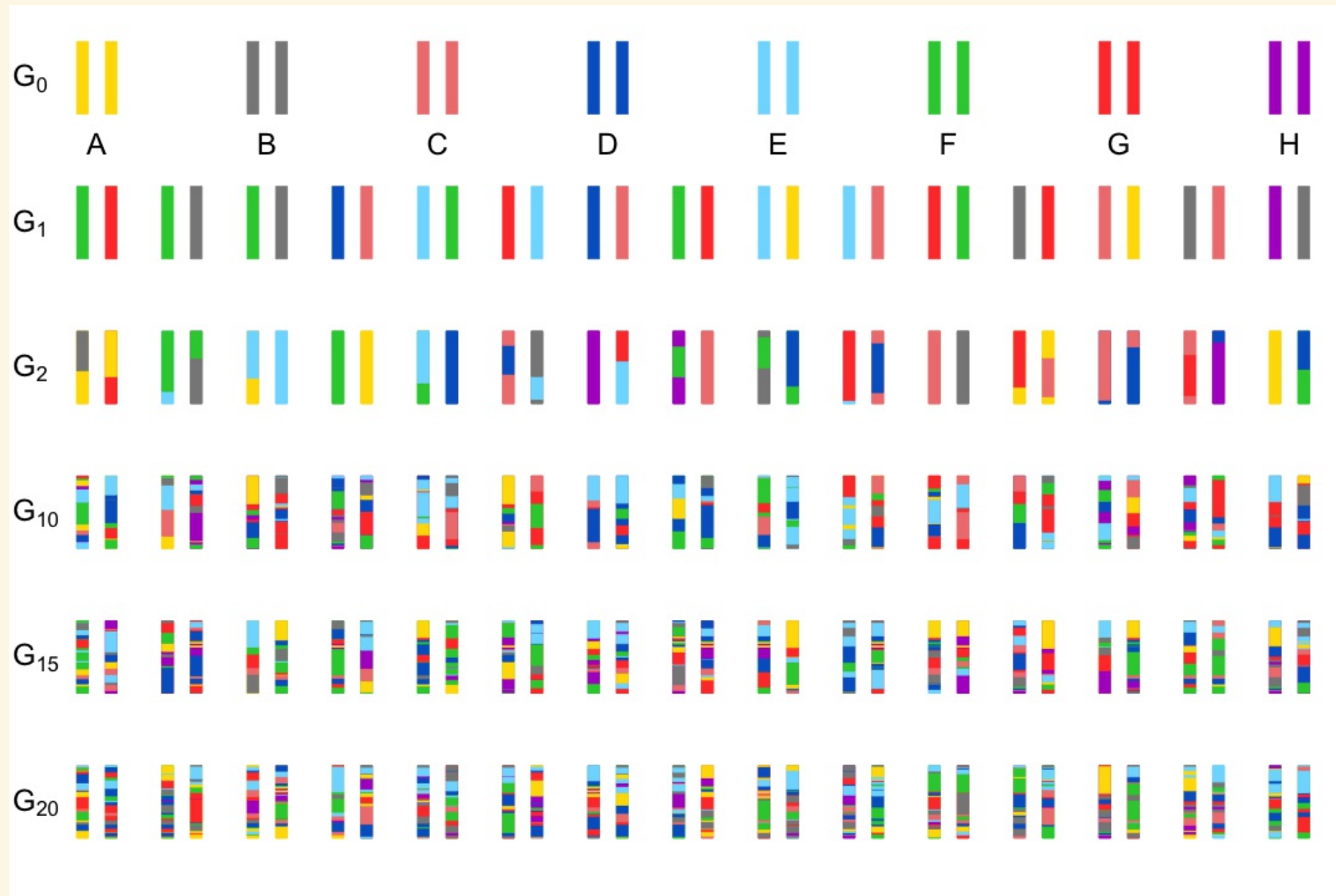
Jiang and Zeng (1995) test

- Perform a two-dimensional two-QTL scan
- $\text{vec}(Y) = X\text{vec}(B) + \text{vec}(E)$
- Calculate likelihood ratio test statistic

Jiang and Zeng (1995) test



Multiparental populations



Challenges in multiparental populations

- Complex patterns of relatedness
- Multiple founder lines

Challenges in multiparental populations

- Complex patterns of relatedness

Multivariate random effects

- Multiple founder lines

Fixed effect for each founder allele

Test procedure

- Model:

$$\text{vec}(Y) = X\text{vec}(B) + \text{vec}(G) + \text{vec}(E)$$

- Calculate likelihoods at every grid point

Test procedure

- Test statistic:

$$-\log \frac{\max(\text{likelihood under pleiotropy})}{\max(\text{likelihood for separate QTL})}$$

- Parametric bootstrap to get a p-value

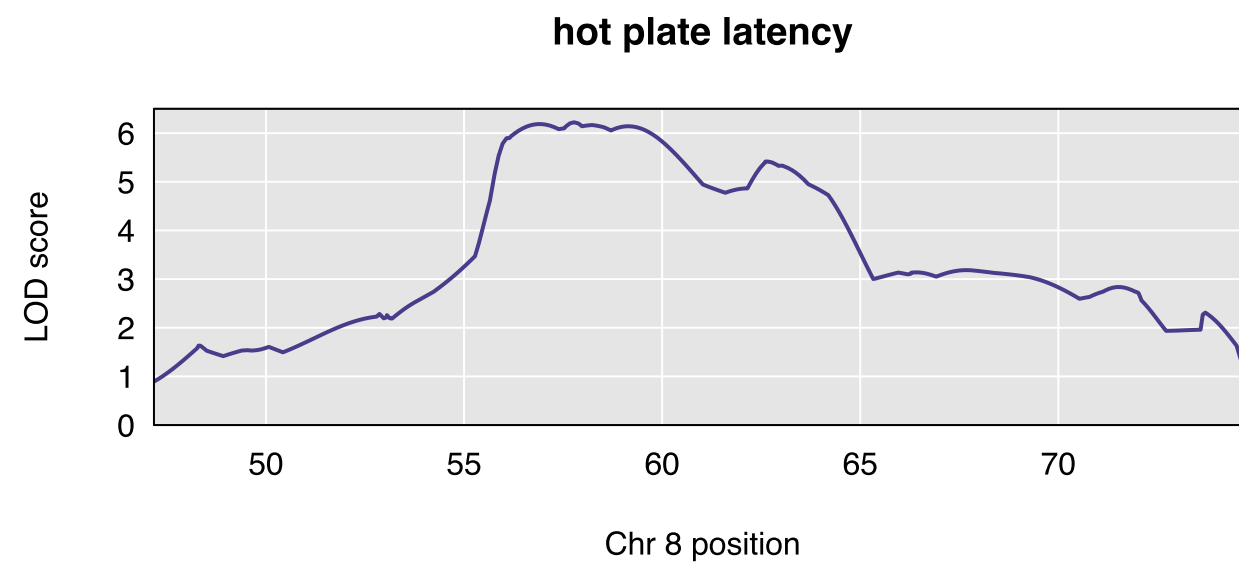
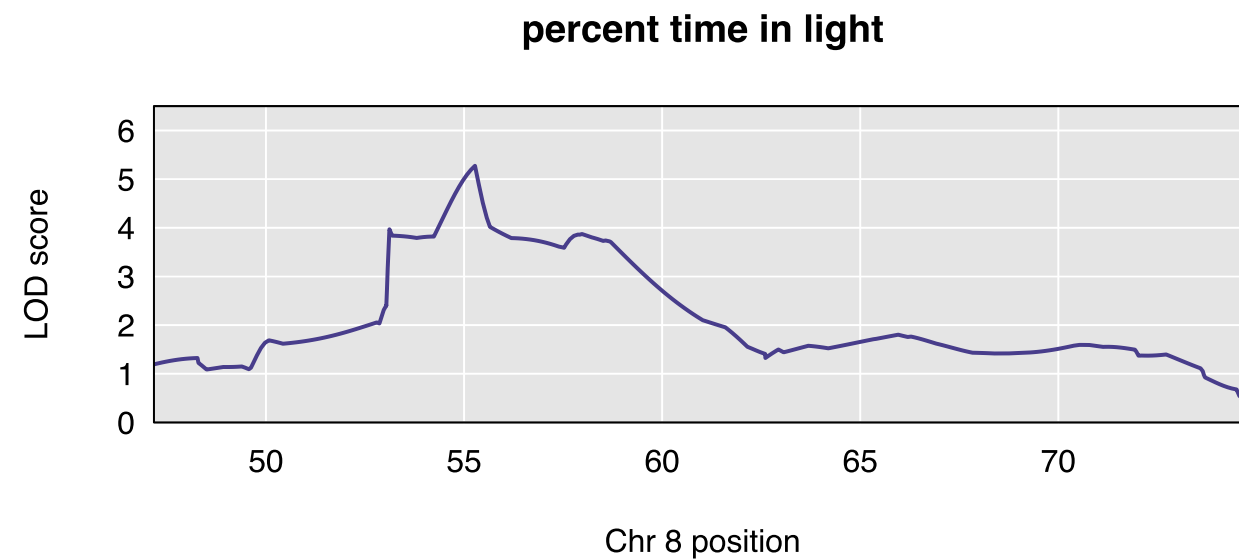
Application

- Logan, et al. (2013) and Recla, et al. (2014) studied 261 Diversity Outbred mice
- Measured about two dozen behavioral traits

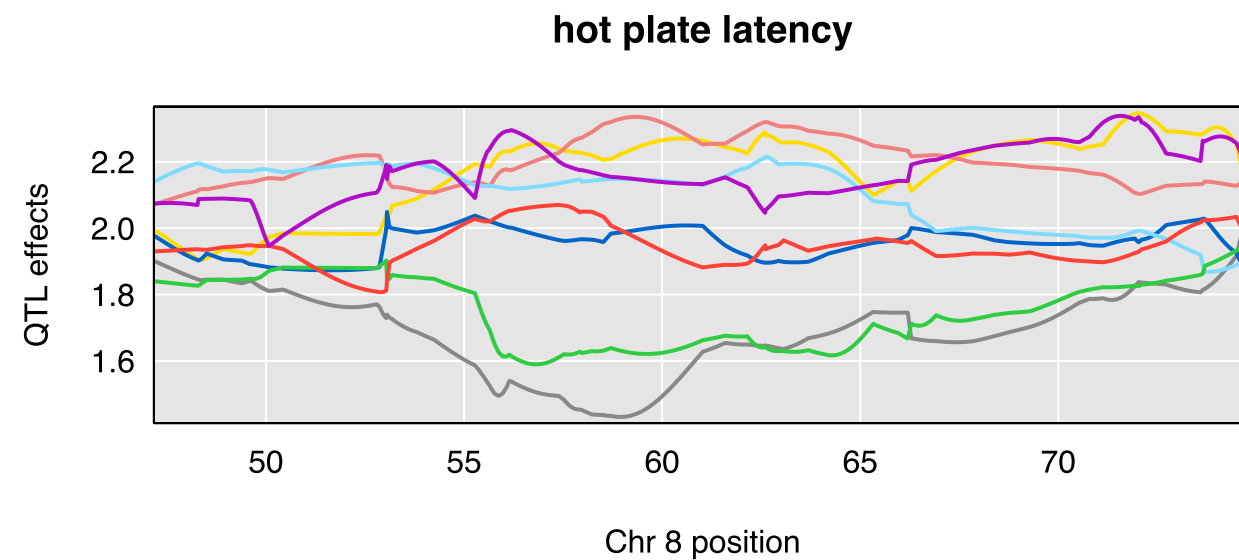
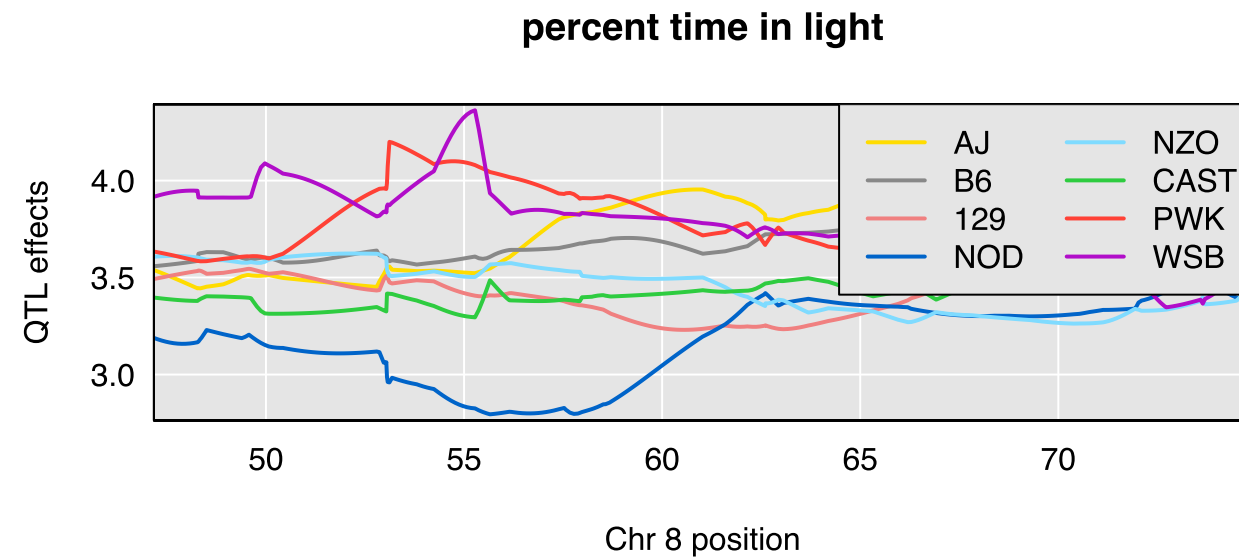
Application

- Two traits map to Chr 8:
 - "hot plate latency" (57 cM)
 - "percent time in light" (55 cM)

QTL scan results

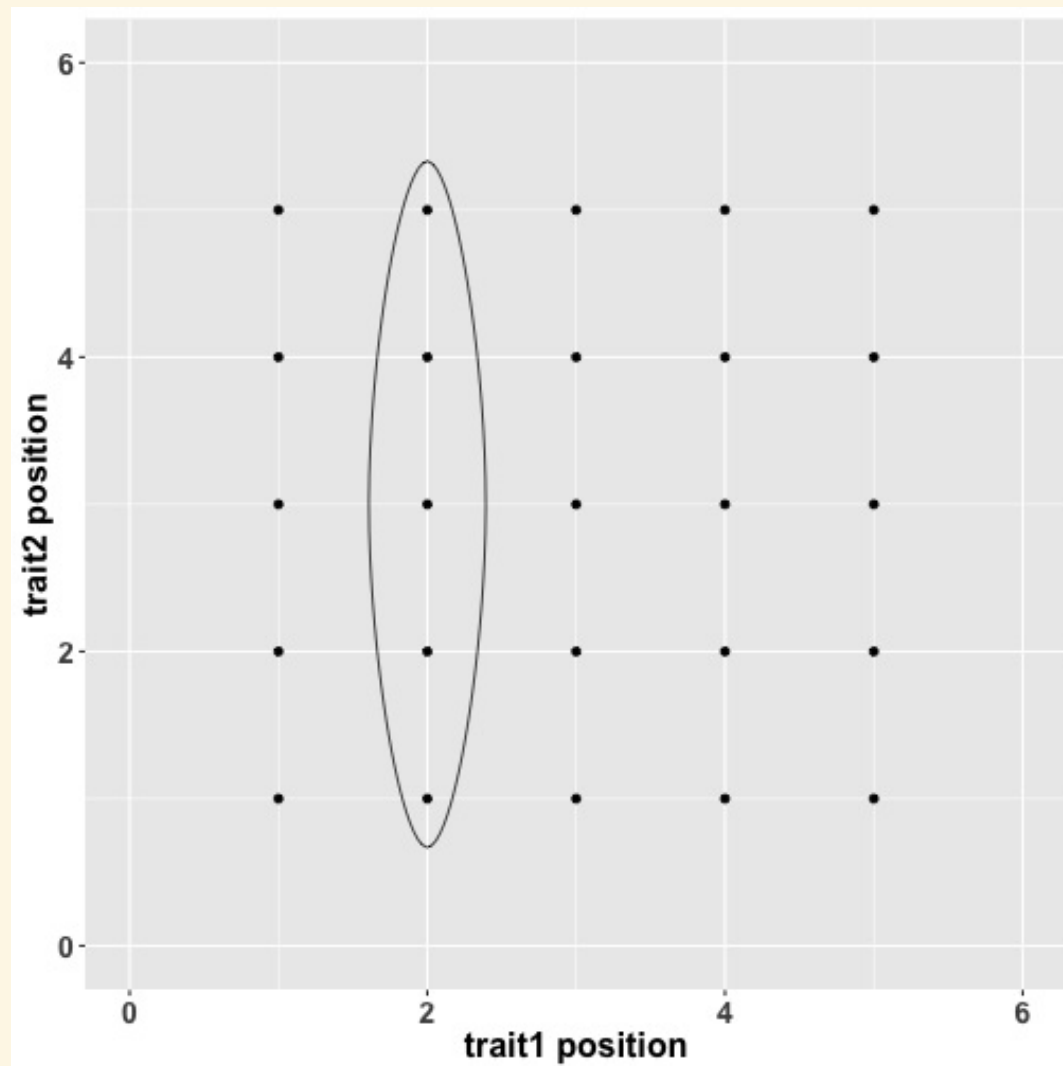


Allele effects plots

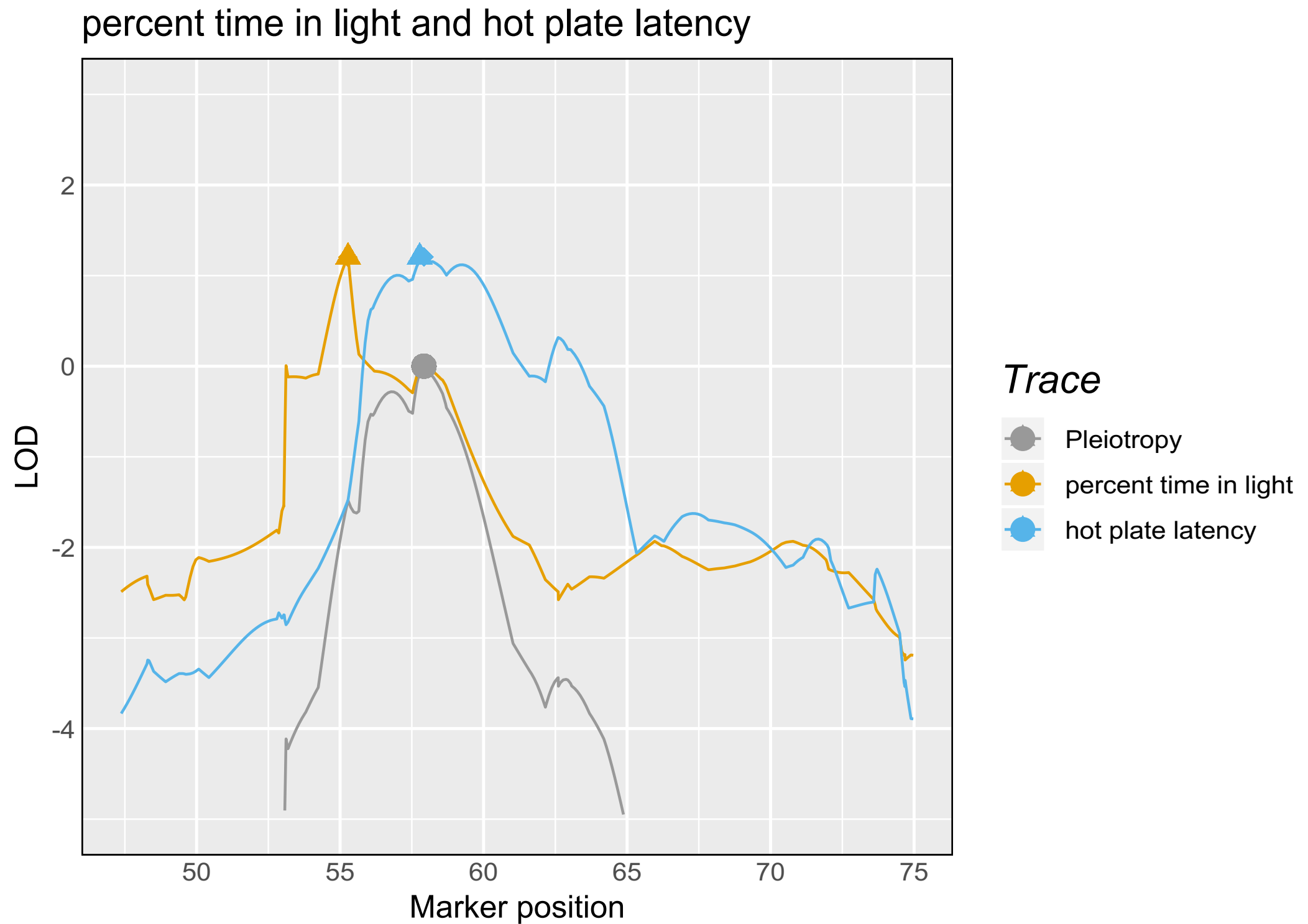


Profile LOD

$$\text{profile LOD}_{\text{trait 1}}(\lambda_1) = \max_{\lambda_2} \text{LOD}(\lambda_1, \lambda_2)$$



Profile LOD



Test results

- $\Lambda = 1.2$
- $p = 0.11$ (1000 bootstrap samples)

Conclusions

- Weak evidence for two separate QTL
 - One QTL affects "distance traveled in light"
 - Second QTL affects "hot plate latency"

Contact information

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- <https://fboehm.us/>
- qtl2pleio R package:
<https://github.com/fboehm/qtl2pleio>
- Biorxiv pre-print: <http://bit.ly/boehm-biorxiv>

References

Jiang, C. and Z. Zeng (1995). "Multiple trait analysis of genetic mapping for quantitative trait loci." In: *Genetics* 140.3, pp. 1111-1127.

Logan, R. W, R. F. Robledo, et al. (2013). "High-precision genetic mapping of behavioral traits in the diversity outbred mouse population". In: *Genes, Brain and Behavior* 12.4, pp. 424-437.

Recla, J. M, R. F. Robledo, et al. (2014). "Precise genetic mapping and integrative bioinformatics in Diversity Outbred mice reveals Hydin as a novel pain gene". In: *Mammalian genome* 25.5-6, pp. 211-222.

References