QTL mapping 4: multivariate phenotypes

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Why multiple phenotypes?

- Might as well measure a bunch of stuff
- Not quite sure what to measure
- Interested in several related features
- Trying to get at intermediate biochemical processes
- What happens over time?
- Reduced measurement error → greater power
Goals

• Use multiple phenotypes to improve QTL detection
• Do traits share QTL (pleiotropy)?
• Causal relationships among traits?
• Effects of QTL across time
Pleiotropy?
Causal?
Basic model

One trait:

\[ y = X\beta + \epsilon, \quad \epsilon \sim N(0, \sigma^2) \]

Multiple traits:

\[ Y = X\beta + \epsilon, \quad \epsilon \sim MVN(0, \Sigma) \]
Basic model

One trait:

\[ y = X\beta + \epsilon, \quad \epsilon \sim N(0, \sigma^2) \]

\[ \text{LOD} = \frac{n}{2} \log_{10}(\text{RSS}_0 / \text{RSS}_1) \]

Multiple traits:

\[ Y = X\beta + \epsilon, \quad \epsilon \sim \text{MVN}(0, \Sigma) \]

\[ \text{LOD} = \frac{n}{2} \log_{10}(|\hat{\Sigma}_0| / |\hat{\Sigma}_1|) \]
Iron levels

The chart shows scatter plots of liver iron levels against spleen iron levels for different groups, indicated by color:
- Red for female
- Blue for male

The iron levels range from 4.5 to 8.0, with specific points marked at 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, and 8.0.
QTL scan

Chromosome vs. LOD score for liver and spleen across various chromosomes.
QTL scan

Chromosome

LOD score

liver
spleen
multivariate
• Consider two traits

• Assume each affected by a single QTL

• Scan chromosome for single QTL, assuming it affects both

• Two-dimensional scan over chromosome, one QTL affecting one trait and other affecting the other trait

• Significance?
  – Parametric bootstrap using fitted single-QTL model
  – Stratified permutation test, permuting within strata defined by genotype at estimated single QTL
Traits over time

- Fit model to each curve; use parameters as phenotypes
- Full QTL model of curves, where parameters depend on QTL genotypes
- Dimension reduction → standard multivariate QTL analysis
- Treat each time point individually, and then combine LOD scores
Gough Island
Big rodents
Big rodents
Big rodents
WSB and Gough mice
Growth curves

Males

Females

Body weight (g) vs. Week
Growth curves

Males

Females
Growth curves

Males

<table>
<thead>
<tr>
<th>Week</th>
<th>Body weight (g)</th>
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Females

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Growth rate

Males

Growth rate (g/week)

Females

Growth rate (g/week)
Growth rate

Males

Females

Growth rate (g/week)

Week
QTL scan for body weight
QTL scan for growth rate