Office hours
3-4pm Wednesdays
304A Stanley Hall

Simulation/theory
Expect 0.09 of a locus to reach LOD=3 by chance.

Not 1-locus dominant, or 1-locus incomplete dominance, or…

Quantitative trait linkage test
Not counting recombinants.
Statistical test for goodness of fit.

>1 locus controlling trait
Just reporting significance of goodness of fit.

What if…
Magnitude of spread within group has not changed.
Locus effect is weaker.
Correct interpretation:

Difference between S and C at this locus has a causal role in blood pressure variation, but effect is modest.

Correct interpretation:

“Effect of having an S allele”

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Most loci underlying human disease look like this.

Complex traits

Just reporting significance of goodness of fit.

Complex traits

Genetic differences at both loci affect the trait.
Complex traits

Each locus responsible for half? Depends on the model.

If 5 loci, each responsible for a fifth? 10 loci? ...

The more loci, the smaller the effects and the harder to detect.

One common result of a linkage study is no significant linkage anywhere.

Genetic complexity is the rule; simple 1- or 2-locus models are the exception.
We haven’t talked about humans lately…

With model organisms, can always study a single cross/family with lots of progeny, so better statistical power to detect weak loci.

And less chance of locus heterogeneity.
**Heritability in exptal organisms**

Why is the green curve taller?

A. There are more mice in the green population
B. More mice in the green population have high blood pressure
C. Fewer differences between mice in the green population
D. Less environmental error/noise in the green population

**Heritability in exptal organisms**

Green = genetically identical, red = genetically different

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**Heritability in exptal organisms**

Genetic variance = total var - “environmental var”

\[ \sigma_g^2 = \sigma_t^2 - \sigma_e^2 \]

“How much of the trait difference between genetically different individuals is due to polymorphisms?”

**Heritability in exptal organisms**

Genetic variance = total var - “environmental var”

\[ \sigma_g^2 = \sigma_t^2 - \sigma_e^2 \]

Heritability \( H^2 = \frac{\sigma_g^2}{\sigma_t^2} \)
Heritability in exptal organisms

Green = genetically identical, red = genetically different

Which trait has a higher heritability?
A. Trait 1
B. Trait 2

Why $h^2$?

“Are DNA differences controlling my trait?”
Otherwise, why bother with genetic mapping?

Heritability in humans: MZ twins

Mean over all = $z$

Heritability in humans: MZ twins

Mean each pair = $z_i$
Heritability in humans: MZ twins

Each individual = \( z_{ij} \)

Mean each pair = \( z_i \)

Total mean sq = \( \sum \frac{\sum (z_{ij} - z)^2}{T} \)

Within pairs mean sq = \( \sum \frac{\sum (z_{ij} - z_i)^2}{N} \)

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“Environment” and genetics

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“Environment” alone
Heritability in humans: MZ twins

Mean each pair = $z_i$

Each individual = $z_i$

Total mean sq = $\frac{\sum (z_i - \bar{z})^2}{T}$

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Between pairs mean sq = $\frac{2 \sum (z_i - \bar{z})^2}{N-1} = \sigma^2 = \sigma^2 + \sigma^2$

Analysis of variance (ANOVA)

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The fraction of the total variance that is attributable to differences between pairs (i.e. is genetic).

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Within pairs mean sq = \[ \sum \frac{(z_{ij} - z_i)^2}{N} = \sigma^2_w \]

\[ \tau^2 = 2[\sigma^2_w(DZ) - \sigma^2_w(MZ)] \]

DZ twins are half as dissimilar as two unrelated people.
Heritability in humans: MZ and DZ

(A more sophisticated model-fitting method)

Adoptee studies

Rates of alcoholism in adopted males

<table>
<thead>
<tr>
<th>Biological parent</th>
<th># in sample</th>
<th>% adopted sons alcoholic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic mother</td>
<td>89</td>
<td>39.4</td>
</tr>
<tr>
<td>Alcoholic father</td>
<td>42</td>
<td>28.6</td>
</tr>
<tr>
<td>Non-alcoholic mother</td>
<td>723</td>
<td>13.6</td>
</tr>
<tr>
<td>Non-alcoholic father</td>
<td>1029</td>
<td>15.5</td>
</tr>
</tbody>
</table>

A qualitative argument for genetic contribution