Two Reasons to Model Phenotype Mean and Variance in QTL Mapping

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Triangle Stat Gen
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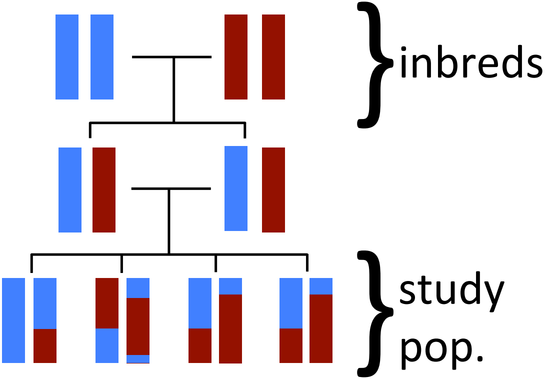
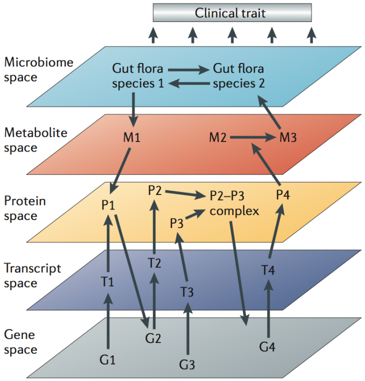
Overview

Background

F2 Intercross Mapping Population



Current Approach to QTL Mapping

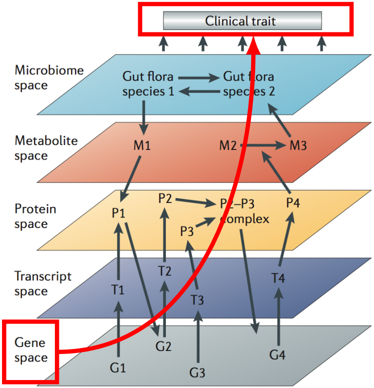


Civelek, 2014

Truth:

$$y_i = f(g_i, t_i, e_i, \ldots)$$

Current Approach to QTL Mapping



Civelek, 2014

Truth:

$$y_i = f(g_i, t_i, e_i, \ldots)$$

Statistical Model:

$$y_i = m_i + \epsilon_i$$

$$\epsilon_i \sim \mathrm{N}(0, \sigma^2)$$

with

$$m_i = \boldsymbol{x}_i^\mathsf{T} \boldsymbol{\beta} + \boldsymbol{q}_i^\mathsf{T} \boldsymbol{\alpha}$$

DGLM Model

Constant variance
QTL Mapping Model:

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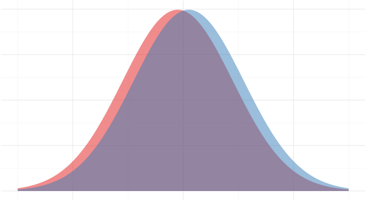

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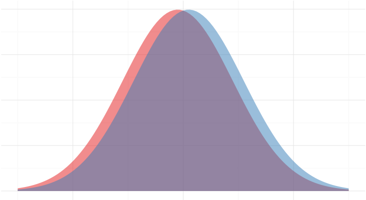


Heterogeneous variance
QTL Mapping Model:

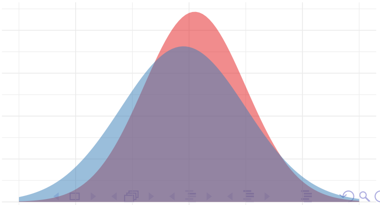
$$y_i = m_i + \epsilon_i$$

$$\epsilon_i \sim \mathrm{N}(0, \exp(v_i)^2)$$

with

$$m_i = \boldsymbol{x}_i^\mathsf{T}\boldsymbol{\beta} + \boldsymbol{q}_i^\mathsf{T}\boldsymbol{\alpha}$$

$$v_i = \boldsymbol{z}_i^\mathsf{T}\gamma + \boldsymbol{q}_i^\mathsf{T}\boldsymbol{\theta}$$



Credits

J. R. Statist. Soc. B (1989)
51, *No.* 1, *pp.* 47–60

Generalized Linear Models with Varying Dispersion

By GORDON K. SMYTH†

University of California, Santa Barbara, USA

DOI: 10.1534/genetics.111.127068

Detecting Major Genetic Loci Controlling Phenotypic Variability in Experimental Crosses

Lars Rönnegård*,[1] and William Valdar[†]

[*]Statistics Unit, Dalarna University, SE-781 70 Borlänge, Sweden and [†]Department of Genetics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-7265

Mean QTL Mapping

Nuisance Variance Heterogeneity

Could some levels of nuisance covariates yield more precise observations than others?

- Technician
- Day
- Apparatus
- Sex of model organism

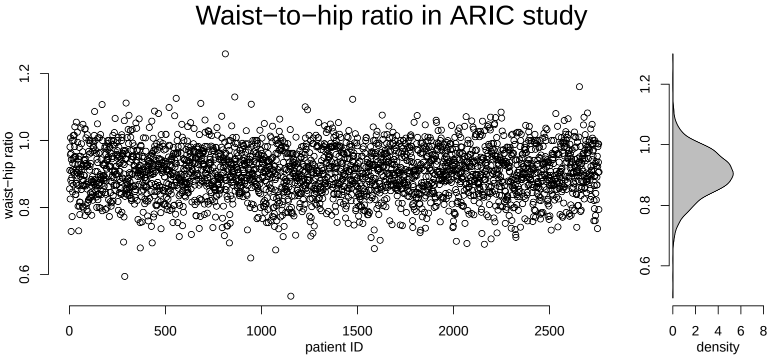
Up-weight those observations.
Down-weight the (otherwise) high leverage points.

Significance vs. Zero-ness

$p > 0.05 \not\Rightarrow \beta = 0$

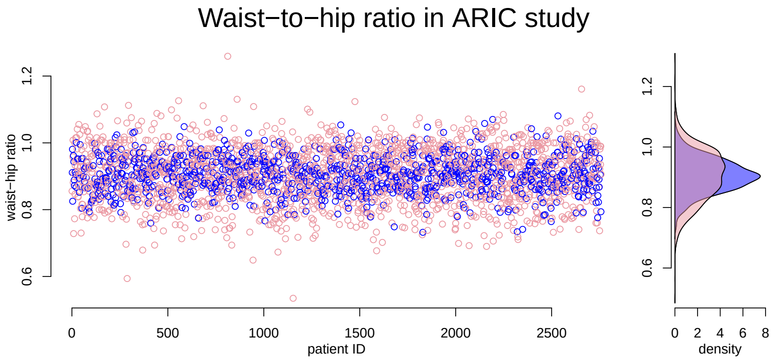
If we wouldn't trust a result that requires excluding some covariate, we should probably model it.

Example 1



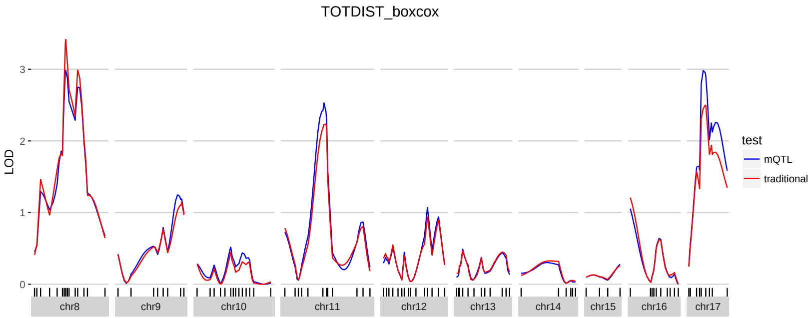
Implications for study design

Example 1



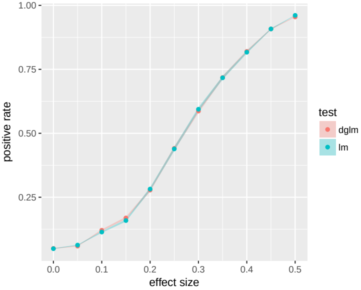
Implications for study design

Example 2

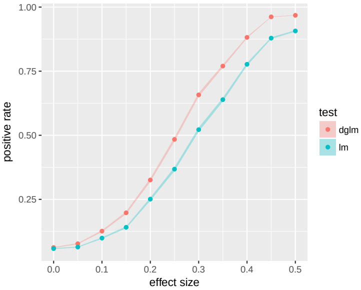

TOTDIST_boxcox
LOD
0
1
2
3
chr8
chr9
chr10
chr11
chr12
chr13
chr14
chr15
chr16
chr17
test
mQTL
traditional

Implications for Power

Homogenous variance scenario:

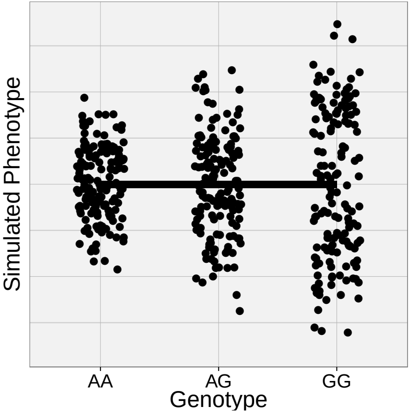


Heterogeneous variance scenario:

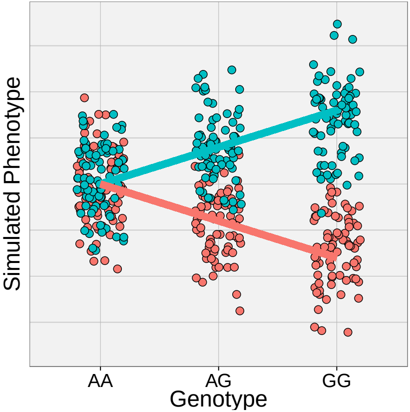


Variance QTL Mapping

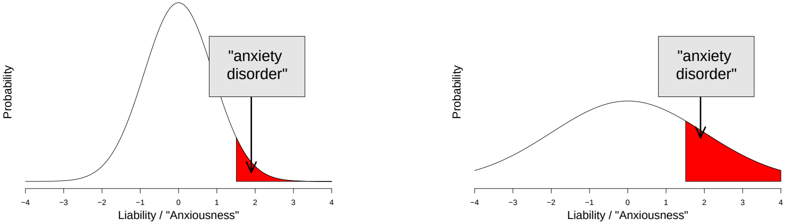
GxE



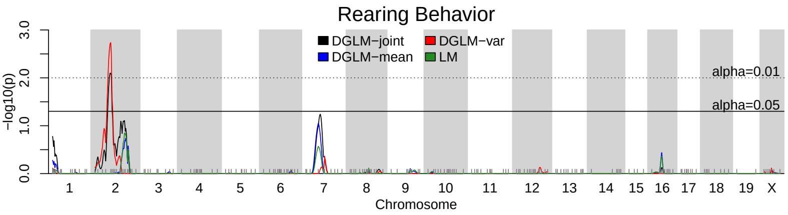
GxE



Liability-Threshold Model



Example 1


Rearing Behavior
DGLM−joint
DGLM−var
DGLM−mean
LM
alpha=0.01
alpha=0.05
−log10(p)
0.0
1.0
2.0
3.0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
X
Chromosome

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Slides: github.com/rcorty/TSG

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