QTL mapping in humans

Karl W Broman
Department of Biostatistics
Johns Hopkins University

www.biostat.jhsph.edu/~kbroman

Linkage vs association

Advantages
+ If you find something, it is real
+ Power with limited genotyping
+ Numerous rare variants okay

Disadvantages
– Need families
– Lower power if common variant and lots of genotyping
– Low precision of localization
• Split mice into groups according to genotype at a marker.
• Do a t-test / ANOVA.
• Repeat for each marker.

Intercross

P₁
×
P₂

F₁
×
F₁

F₂

ANOVA at marker loci

Genotype at D14Mit54
SS BS BB

Genotype at D16Mit30

Genotype at D14Mit54
Human pedigree

Sibling pairs
Humans vs mice

- More than two alleles
- Unknown phase
- Parents may be homozygous
- Markers not fully informative
- Varying environment

Diallelic QTL
Identity by descent

IBD = 1

IBD = 1 or 2

IBD = 2
IBD = 1 or 2

Challenges

- Non-normality
- Genetic heterogeneity
- Environmental covariates
- Multiple QTL
- Multiple phenotypes
- Complex ascertainment
- Precision of mapping