1. why study multiple traits together?

- avoid reductionist approach to biology
  - address physiological/biochemical mechanisms
  - Schmalhausen (1942); Falconer (1952)
- separate close linkage from pleiotropy
  - 1 locus or 2 linked loci?
- identify epistatic interaction or canalization
  - influence of genetic background
- establish QTL x environment interactions
- decompose genetic correlation among traits
- increase power to detect QTL

interplay of pleiotropy & correlation

pleiotropy only

Korol et al. (2001)

correlation only

both
3 correlated traits
(Jiang Zeng 1995)

ellipses centered on genotypic value
width for nominal frequency
main axis angle environmental correlation
3 QTL, F2
27 genotypes

note signs of
 genetic and
environmental
correlation

pleiotropy or close linkage?

2 traits, 2 qtl/trait
pleiotropy @ 54cM
linkage @ 114,128cM
QTL with GxE or Covariates

- adjust phenotype by covariate
  - covariate(s) = environment(s) or other trait(s)
- additive covariate
  - covariate adjustment same across genotypes
  - “usual” analysis of covariance (ANCOVA)
- interacting covariate
  - address GxE
  - capture genotype-specific relationship among traits
- another way to think of multiple trait analysis
  - examine single phenotype adjusted for others

R/qtl & covariates

- additive and/or interacting covariates
- test for QTL after adjusting for covariates

```r
## Get Brassica data.
library(qtlbim)
data(Bnapus)
Bnapus <- calc.genoprob(Bnapus, step = 2, error = 0.01)

## Scatterplot of two phenotypes: 4wk & 8wk flower time.
plot(Bnapus$pheno$log10flower4,Bnapus$pheno$log10flower8)

## Unadjusted IM scans of each phenotype.
f18 <- scanone(Bnapus,, find.pheno(Bnapus, "log10flower8"))
f14 <- scanone(Bnapus,, find.pheno(Bnapus, "log10flower4"))
plot(f14, f18, chr = "N2", col = rep(1,2), lty = 1:2,
     main = "solid = 4wk, dashed = 8wk", lwd = 4)
```
R/qtl & covariates

- additive and/or interacting covariates
- test for QTL after adjusting for covariates

## IM scan of 8wk adjusted for 4wk.
## Adjustment independent of genotype
f18.4 <- scanone(Bnapus, find.pheno(Bnapus, "log10flower8"),
                   addcov = Bnapus$pheno$log10flower4)

## IM scan of 8wk adjusted for 4wk.
## Adjustment changes with genotype.
f18.4 <- scanone(Bnapus, find.pheno(Bnapus, "log10flower8"),
                   intcov = Bnapus$pheno$log10flower4)

plot(f18, f18.4a, f18.4, chr = "N2",
     main = "solid = 8wk, dashed = addcov, dotted = intcov")
scatterplot adjusted for covariate

```r
## Set up data frame with peak markers, traits.
markers <- c("E38M50.133","ecn2e5a","wg7f3a")
tmpdata <- data.frame(pull.geno(Bnapus)[,markers])
tmpdata$fl4 <- Bnapus$pheno$log10flower4
tmpdata$fl8 <- Bnapus$pheno$log10flower8

## Scatterplots grouped by marker.
library(lattice)
xyplot(fl8 ~ fl4, tmpdata, group = wg7f3a,
col = "black", pch = 3:4, cex = 2, type = c("p","r"),
xlab = "log10(4wk flower time)",
ylab = "log10(8wk flower time)",
main = "marker at 47cM")
xyplot(fl8 ~ fl4, tmpdata, group = E38M50.133,
col = "black", pch = 3:4, cex = 2, type = c("p","r"),
xlab = "log10(4wk flower time)",
ylab = "log10(8wk flower time)",
main = "marker at 80cM")
```

R/qtlbim and GxE

- similar idea to R/qtl
  - fixed and random additive covariates
  - GxE with fixed covariate
- multiple trait analysis tools coming soon
  - theory & code mostly in place
  - properties under study
  - expect in R/qtlbim later this year
  - Samprit Banerjee (N Yi, advisor)