

BIS101 F2013 Lecture 5: Quantitative Traits

qualitative traits

- red or green, wrinkled vs. round, etc.
- discrete states
- usually simple genetic basis -- one or two genes

quantitative traits

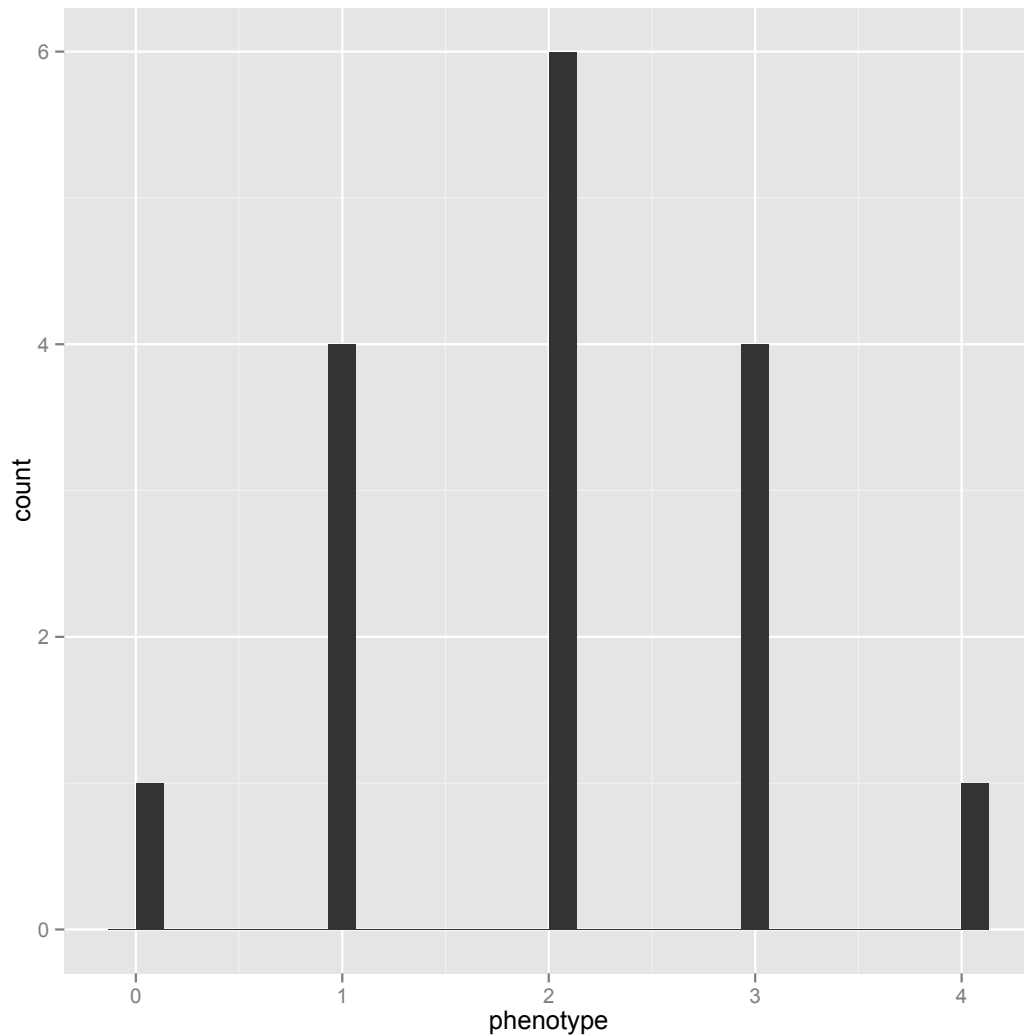
- height, IQ, etc. not discrete
- usually complex genetic basis -- many genes or QTL
- each QTL is a normal Mendelian locus, but their effects combine to form phenotype
- Simple example w/ two loci. each big allele adds 1 to phenotype

A cross AABB with aabb and look at F2 (draw out A's and B's). Showing possible genos/phenos,

A locus	B locus	Phenotype
1 1	1 1	4
1 1	1 0	3
1 1	0 1	3
1 1	0 0	2
1 0	1 1	3
1 0	1 0	2
0 1	1 0	2
1 0	0 1	2
0 1	0 1	2
1 0	0 0	1
0 1	0 0	1
0 0	1 1	2
0 0	1 0	1
0 0	0 1	1
0 0	0 0	0

but there will be 2 of each het (1:2:1 Mendel), so distribution of phenos will be:

and it looks like (draw):

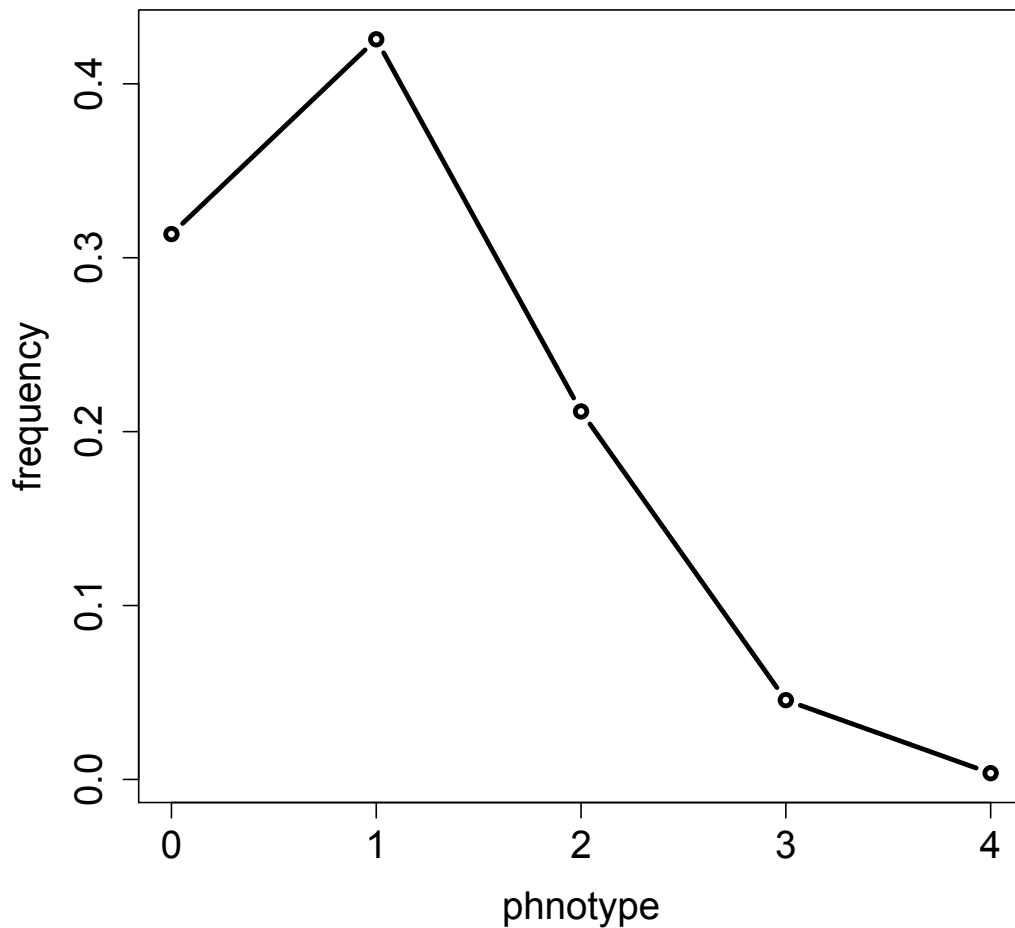


As you get more and more loci, becomes normal.

This is for a cross where at each het we have 1:2:1 segregation in F2, but in a population what determines the distribution ??? (allele freqs, which we talk about next time)

Popgen! So distribution would be freq. of genotype * value, e.g.

@ locus A $p_A=0.2$ and at locus B $p_B 0.3$



Most phenotypes of interest are quantitative.

- Even color (how much of the pigment)
- Disease: Diabetes not all the same

Statistically, you assume a quant. trait is controlled by an infinite number of genes

- obv. not infinite, but in many cases (human height) it's probably hundreds or thousands
- not all have to have same effect as above. e.g fw2.2 tomato size
- but each gene here isn't special. can have different effect size, but all follow Mendel.

Phenotypic variation

The equation: $V_P = V_G + V_E$ (what is variance?)

- V_P we can measure: $\sum(x - \bar{x})^2/n$
- explain genetic variance, what is environmental variance

Redraw histogram w/ variation around values due to environment.

- e.g. take identical twin mice and I give one lots of food, and the other none. V_E will determine all of phenotypic difference!

Heritability

$H^2 = V_G/V_P$ = broad sense heritability

heritability is the % of phenotypic variation due to variation in genes

- NOT whether or not a trait varies
- NOT whether or not it's genetic
 - e.g. fitness in natural populations
 - in humans reproduction: lots of choice/culture/economy going into how many kids
 - doesn't mean ability to reproduce is not genetic, just that much of the variance is V_E
 - keep the genes the same, but increase environmental variance, heritability goes down
- NOT explain between group differences
 - because environments may differ & depends on environ
 - if we take mouse weight, heritability in mouse weight will differ in an environment where mice are starved and in an environment where there is lots of food (perhaps)
- NOT % due to genes
 - 80% narrow sense heritability for height NOT mean 20% of your height is environmental
 - means 20% of the total variation seen among population is due to environment
- even when high, doesn't mean all change due to genes
 - Dutch height has increased maybe 16cm over last 150 years
 - not very long for nat. selection to work (~7 generations)
 - probably mostly due to improved health care, food, etc.
- V_G may change as allele frequencies change (popgen)

How to estimate

One way to estimate broad sense, in humans, is looking at twins separated.

Genes identical, environment diff. Similarity must be due to genes.

Covariance in phenotype: $(\sum(X - \bar{X})(Y - \bar{Y}))/n$ <- first and second twin

From twin studies:

Trait	H ²
Height	0.88
Waist circumference	0.25
IQ	0.69
alcoholism	0.5
autism	0.9
religiosity	0.4

Additive genetic variance

$$V_G = V_A + V_D + V_I$$

- V_A additive -- stuff we most care about b/c responds easily to selection and easy to model and work with, dominance, interaction b/t genes)

$h^2 = V_A/V_P$ = narrow sense heritability -> can calculate from phenotypic means of progeny

narrow sense is what geneticists care about, what responds to selection, etc.

Think about selecting on a phenotype -- selection wants bigger mouse:

AA 20 cm Aa 15 cm aa 10 cm

Selection is easy.

AA 20 cm Aa 20 cm aa 10 cm

Selection doesn't work as well because brings along a little a with many of the big A.

Can estimate heritability by covariance between parents and offspring

- same environment, offspring inherit 1/2 genes from parent
- so $\text{COV}(p-o) = 1/2 V_A$

Breeder's equation

$$R = h^2 * S$$



If you know heritability (from some other estimate) you can predict response to selection on quant. trait

Different from response to selection on a single locus (what we will talk about in popgen)

But also if I select on a trait, can use response to estimate narrow sense heritability.

What does low h^2 mean? means that won't respond to selection well b/c most of phenotype is not due to additive genetic effects

Mapping QTL

looking for statistical association between a genetic marker and a phenotype

Draw cross between fluffy rabbit and hairless rabbit

- draw 1 pair of chromosomes w/ markers
- phenotype varying among offspring
- statistical association that everytime you see marker X, ~10% fluffier

M1	M2	M3	M4	Phenotype
MM	Mm	Mm	mm	3.89
Mm	Mm	mm	Mm	1.29
MM	mm	Mm	Mm	3.63
mm	MM	MM	Mm	5.42
MM	Mm	Mm	mm	3.37
Mm	MM	mm	MM	1.99
Mm	mm	Mm	mm	3.05
MM	mm	Mm	MM	3.91
mm	Mm	MM	Mm	5.26
mm	Mm	mm	mm	1.04
-0.02	0.01	0.97	0.1	

Can you cross 2 parents w/ same phenotype and get variation?

- yes, think two people exactly 5'7"
- Example w/ our two locus system: $AAbb = 10$ and $aaBB = 10$ and $AABB = 20$ and $aabb = 0$.

Parents can harbor alleles that don't make initial sense

- $AABBcc \times aabbCc$ (4 x 1 phenotype)
- new allele in low parent that not present in high parent!

Since crosses and linkage mapping are hard in some organisms (humans), we do association

mapping. Also seen as GWAS -- genome wide association study.

Genotype a large number of unrelated individuals and look for the correlation there