Heritability

The concept
What is the Point of Heritability?

- Is a trait due to nature or nurture?
  - (Genes or environment?)
- You and I think this is a good point to address, but it is *not* addressed!
- What is addressed is:
  
  Is *variation* in a trait due to nature or nurture?
  
  - (review: genes, environment, nature, nurture — which are more synonymous)
What is the Point of Heritability?

• Is a trait due to nature or nurture?
  vs.
• Is variation in a trait due to nature or nurture?

• Which is better for what purposes?
• How can these be investigated?
• Why is variation used with heritability in the technical sense?
It's not that Intuitive …

• Does # fingers have
  - High heritability, or
  - Low heritability?
It's not that Intuitive …

- Let's look at the genomes of some organisms that
  - know a lot about bioinformatics, and
  - know very little about bioinformatics
Is knowledge of bioinformatics highly heritable?

Sample organisms that know a lot about bioinformatics

Sample organisms that know little about bioinformatics

Is knowledge of bioinformatics highly heritable?
Break Phenotypic Variance into Two Parts

- \( S_p^2 = S_e^2 + S_g^2 + 2\text{cov}(e, g) \)

- If we can assume \( e \) and \( g \) are independent...

- \( S_p^2 = S_e^2 + S_g^2 \)

- Can we assume independence?
- Which variable(s) do we solve for?
Some Statistical Background

• What is the variance of a single coin toss?
  - \( S^2 = \)
  - Expectation of squared deviation from the mean
  - Let's work it out …

  (& keep results on board for later reference)
Some Statistical Background

- What is the variance of a double coin toss?
  - $S^2 =$
  - Expectation of squared deviation from the mean
  - Let's work it out ...
Some Statistical Background

- What is the covariance of a double coin toss -
  - if the tosses are independent
  - If the tosses are completely dependent
  - Covariance = (x-e(x))*(y-e(y))
    - (this expression is part of the formula for Pearson correlation)
  - Let's work it out ...
Some Statistical Background

• What is the variance of a double coin toss?
• \((2^{\text{nd}} \text{ coin carefully set to be same as } 1^{\text{st}})\)
  - \(S^2 = \)
  - Expectation of squared deviation from the mean
  - Let's work it out ...
Phenotypic variation due to variation in
- genotype
- environment

Top speed of rat when approached by massage therapist
Break Phenotypic Variance into its Two Parts

- \( S_p^2 = S_e^2 + S_g^2 + 2\text{cov}(e, g) \)

- If we can assume \( e \) and \( g \) are independent...

- \( S_p^2 = S_e^2 + S_g^2 \)

- Can we assume independence?
- Which variable(s) do we solve for?
Defining Heritability ($H^2$)

• The fraction of phenotypic variance arising from genotypic variance

• Using $S_p^2 = S_e^2 + S_g^2$ ...
  - What would the formula for heritability be?
Defining Heritability ($H^2$)

- The fraction of phenotypic variance arising from genotypic variance
  - Griffiths et al.: this is "broad sense heritability"

- Using $S_p^2 = S_e^2 + S_g^2$ ...
  - What is the formula for (broad) heritability?
Narrow Sense Heritability

• Broad sense heritability: $H^2$
• $S_g^2 / S_p^2$
  • (where $S_p^2 = S_e^2 + S_g^2$)
• There is also narrow sense heritability
  • $S_a^2 / S_p^2$, $S_g^2 = S_a^2 + S_d^2 + S_i^2$
    - a for additive, d for dominance, i for interactive genetic variance

- Which is higher, broad or narrow sense heritability?
Narrow Sense Heritability (ii)

- There is also narrow sense heritability
  \[ \frac{S_a^2}{S_p^2}, \quad S_g^2 = S_a^2 + S_d^2 + S_i^2 \]
  - a for additive, d for dominance, i for interactive genetic variance

- Variances due to genetic differences adds by “default”
  - (many genes act more or less independently)
Narrow Sense Heritability (ii)

- There is also narrow sense heritability

\[ \frac{S_a^2}{S_p^2}, \quad S_g^2 = S_a^2 + S_d^2 + S_i^2 \]

- a for additive, d for dominance, i for interactive genetic variance


- Variances when one gene is dominant do not add

- Some genes affect one another in other ways
  
  - *i* for “epistatic” (actually for “interactive”)
Back to Broad Sense
Heritability ($H^2$)

- Let's apply this concept to twin studies
  - See http://en.wikipedia.org/wiki/Twin_study
  - See http://en.wikipedia.org/wiki/Falconer\'s\_formula
  - See review paper:
    http://d.yimg.com/kq/groups/20928795/253004760
Broad sense heritability: $H^2$

- $S_g^2 / S_p^2$
  
  - (where $S_p^2 = S_e^2 + S_g^2$)

- “… heritability in one population does not, in theory, predict the heritability of the same trait in another population”
  

- Why?

- But in practice, the heritabilities are often similar
  
  - Exception: heritability often is higher in good environments
Application: Artificial Selection

- $S_g^2 / S_p^2$
  
  - (where $S_p^2 = S_e^2 + S_g^2$)

- We want higher yielding corn, more milk from cows, faster (more efficient) meat growth
  
  - Surely growing meat in a vat is potentially even more efficient...)

- This leads to the breeder's equation
Breeder's Equation

- $R = h^2 \times S$
  - $R$—response to selection
    - (change in phenotypic mean from parents to offspring)
  - $S$—selection differential
    - (deviation from phenotypic mean of the average of the parents)
Selection, heritability, and environment

- Heritability tends to be higher in good environments
- See Figure 1 in Visscher et al.
  - Bird tarsus length:
    - $h^2 = \text{about 0.6 in a good environment}$
    - about 0.4 in a poor one
- Various other cases
Another way to determine heritability

- See figure 2 in Visscher et al.
  - Graph $R$ vs. $S$
  - Draw a regression line
  - Slope is the heritability
- Error around regression line in the figure is higher for the low heritability case
  - Why?
  - Is this intrinsic?
Twin Study Heritability ($H^2$)

- Compare identical twins (monozygotic) with fraternal twins (dizygotic)
  - Fraternal twins must have the same gender

- We'll transfer the variance idea to correlation
  - Closely related concepts –
    - The Pearson correlation definition uses variance
Twin Study Heritability ($H^2$)

- Identical twins – monozygotic – mz
- Fraternal twins – dizygotic – dz
- Correlation values go from 0 (none) to 1 (high)
  - Measure the correlation of a trait among MZ
    - Part of it is due to genetics (A)
    - Part of it is due to shared environment C
    - $r_{mz}=A+C$
  - Measure the correlation of the trait among DZ
    - $r_{dz}=A/2 + C$
    - ...since they share half their genes
Twin Study Heritability ($H^2$)

- Identical twins – monozygotic – mz
- Fraternal twins – dizygotic – dz
- Correlation values $r$ go from 0 (none) to 1 (high)
  - Amount of correlation due to genetics (A)
  - Amount due to shared environment (C)
  - $r_{MZ}=A+C$  $r_{DZ}=A/2 + C$
  - Now we can (easily) solve for A!
Twin Study Heritability ($H^2$)

- Identical twins – monozygotic – mz
- Fraternal twins – dizygotic – dz
- Correlation values $r$ go from 0 (none) to 1 (high)
  - Effect on the results of differing environments is $E$
    - Even identical twins always have differing environments (like what?)
    - If $E$ was 0, $r_{mz}$ would be 1 (why?)
    - So $E=1-r_{mz}$
- We've now solved for A and E, but not yet C
Twin Study Heritability ($H^2$)

- Identical twins – monozygotic – mz
- Fraternal twins – dizygotic – dz
- Correlation values $r$ go from 0 (none) to 1 (high)
  - Recall $r_{mz} = A + C$
  - So $C = r_{mz} - A$
- We've now solved for
  - Genetic contribution to correlation
  - Shared environmental contribution
  - Correlation missing due to differing environment
What Heritability Tells Us

- It says how much of the variation in phenotype is due to genetic variation
  - Is this about groups, individuals, or both?
- Does it say anything about causality?
- Are 9 of your fingers from genes, 1 from environment?
- Is 50% of your longevity from genes, 50% from environment?
What Heritability Tells Us

● Suppose phenotypic variance is greater in more genetically diverse groups
  - Does this mean genes influence the trait in question?

● Suppose phenotypic variance is the same for groups of different genetic diversity
  - Does this mean genes do not influence the trait in question?
What Heritability Tells Us

• Suppose phenotypic variance is greater in more genetically diverse groups
  − Does this mean genes influence the trait in question?
    • Yes

• Suppose phenotypic variance is the same for groups of different genetic diversity
  − Does this mean genes do not influence the trait in question?
    • Recall the # fingers example
    • Another case: genetic diversity was 0
What Heritability Tells Us

- "In general, the heritability of a trait is different in each population and in each set of environments [sic]; it cannot be extrapolated from one population and set of environments to another." - Griffiths et al., 2000
What Heritability Tells Us

- Can genes be relevant to a trait, and genetic variance be irrelevant to trait variance?

- Can genes be irrelevant to a trait, and genetic variance be relevant to trait variance?
What Heritability Tells Us

• Suppose variations in a gene matter in one environment but not another
  – Human blood type?

• Then genotypic variance (e.g. in blood type)
  – Statistically "explains" variance in health/death
    • More in one environment than the other
    • Health/death is more heritable in one environment than the other!

• So heritability is very relative
• The number has little intrinsic meaning if someone calculates that, for example,
  – Intelligence has a heritability of 0.4 (or whatever)
What Heritability Tells Us

- Griffiths et al.: "Summary measures such as $H^2$ are not first steps toward a more complete analysis and therefore are not valuable in themselves."

Vissher et al.:
- “...it allows … *comparison* of the same trait across populations and of different traits within a population.”
- (Emphasis added)
What Heritability Tells Us

- Vissher et al.:
  
  “... heritability remains key to the response to selection in evolutionary biology and agriculture, and to the prediction of disease risk in medicine.”
Note to instructor: add more points from Visscher paper as noted in hard copy starting from p. 261 except fig. 2 already discussed herein