Overview

- Overdominance
- Underdominance
- Evolution fails to optimize
- Frequency-dependent selection

Administrative issues

- Don't forget class is now at 11:00-12:00!
- Corrected version of HW2 (with data table) now up on web site
- Corrected version of lec5 notes (coherent problem among slides) also up

From the one-minute responses

- A concrete selection coefficient example would be nice

Selection coefficient

- In flies, vg/vg genotype has vestigal wings; the trait is fully recessive
- In high school, I put 50 heterozygous $+/vg$ flies in a bottle and counted adult offspring
- I got something like:

Phenotype	wild-type	vestigal
Observed	89	11

- What is the selection coefficient against vg/vg?

Selection coefficient

Phenotype	wild-type	vestigal
Observed	89	11
Expected	75	25
Raw fitness	1.187	0.44
Normalized	1.00	0.37

- $1 - s = 0.37$
- $s = 0.63$
- This is the relative disadvantage of vg/vg (the bigger, the worse)
- Note that I had to assume $+/+$ and $+/vg$ have the same fitness, as I couldn't tell them apart....
- (I had too much water in the fly medium; wingless flies were drowning)

Overdominance (heterozygote advantage)

- Fitness of heterozygote greater than either homozygote
- Note that this is not a kind of dominance! (Dominance is about the *phenotype* of the heterozygote; this is about the *fitness*)
- Controversy: how common is this?

Overdominant math

Helpful to write the fitnesses as:

AA	Aa	aa
1-s	1	1-t

- In an overdominant locus s and t are both positive
- This has an equilibrium at $p = t/(s + t)$

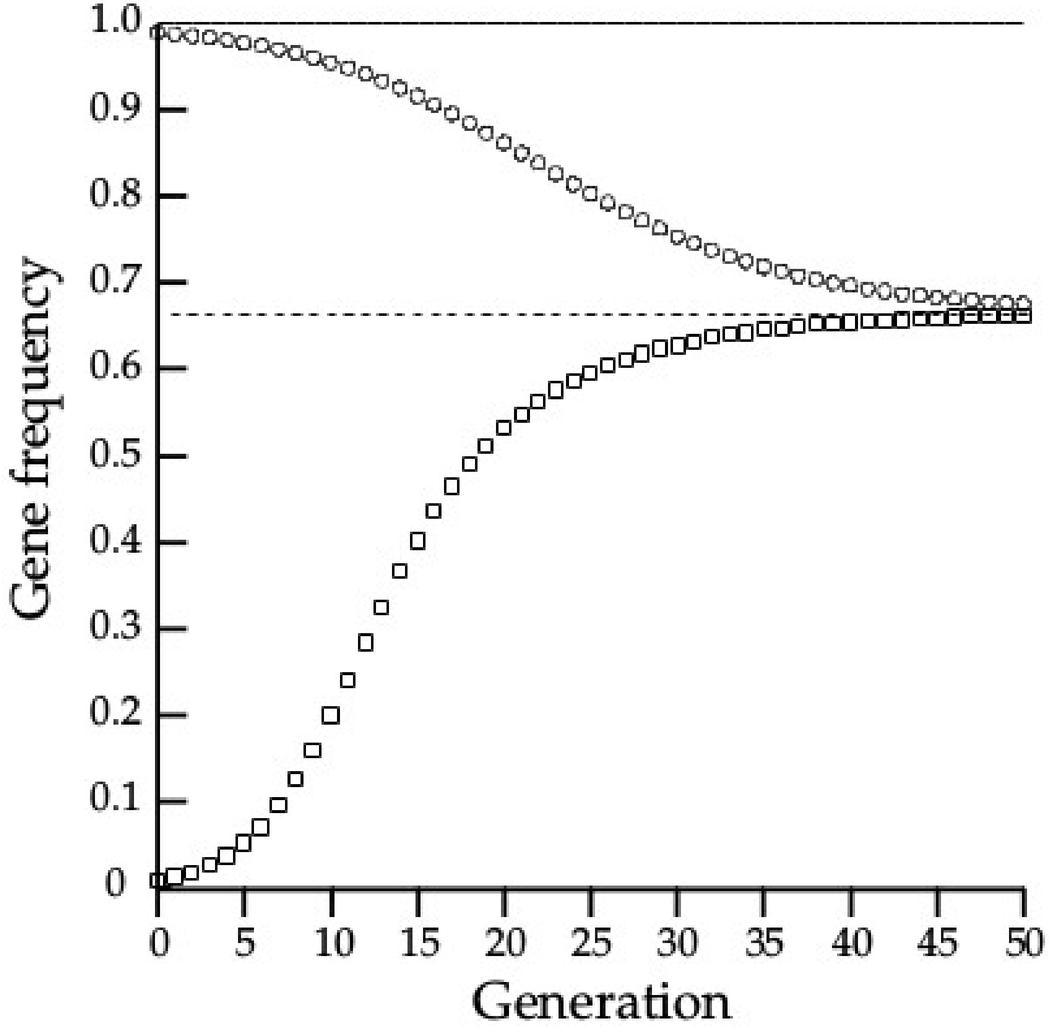

Figure 2.5: Convergence of initial gene frequencies from $p_A = 0.99$ and $p_a = 0.01$ to equilibrium when the fitnesses of *AA*, *Aa*, and *aa* are 0.85 : 1 : 0.70

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Overdominant equilibrium

- This is a stable equilibrium–the population returns if perturbed
- Implications:
  - The better allele is more frequent at equilibrium
  - Mean fitness of the population is less than 1 at equilibrium
  - Both alleles persist in the population forever, barring drift
- At the overdominant human locus *HLA-DRB1* the MRCA of some human alleles lies in the common ancestor of humans, chimps and gorillas

Resolving overdominance

- In squirrel monkeys, red and green color vision are alleles
- The locus lies on the X chromosome:

Genotype	Phenotype
$X^g X^g$, $X^r X^r$	Dichromat female
$X^g X^r$	Trichromat female
$X^g Y$, $X^r Y$	Dichromat male

- Selection for the trichromat phenotype can never fix it
- Max frequency of trichromat females is 0.5
- (UW researchers produced functional trichromat males by gene therapy in adult animals, a shocking result!)

Resolving overdominance

- In humans, the locus is duplicated
- One copy is fixed for X^g and one for X^r
- Both sexes are trichromats
- If trichromats are favored, the fitness of the population would be improved by such a gene duplication
- (The loci are adjacent, which makes them unstable, leading to a high frequency of colorblindness in male humans–more on this later)

Something else can masquerade as overdominance

- Crosses between breeds and species often very fit ("hybrid vigor", "heterosis")

- Could be due to overdominant loci

- Could also be due to fixed bad recessives:
  - Two loci, bad alleles a and b
  - Breeds are fixed for $AAbb$ and $aaBB$
  - Hybrids are $AaBb$ and are more fit

- Discussion: how to tell these possibilities apart?

Overdominance with more than 2 alleles

- Systems with 3+ alleles for which all heterozygotes are better than the associated homozygotes can be stable

- As the number of alleles involved increases, the equilibrium becomes more fragile
  - If many alleles are already present, homozygotes become rare; adding another allele has little effect
  - Eventually alleles tend to drop out due to drift

Top alleles at *HLA-DRB1*

Allele	Frequency worldwide	Regions where found
1501	0.079	11/11
0701	0.070	11/11
0301	0.068	11/11
1101	0.059	10/11
1101	0.055	10/11
1101	0.048	11/11
1101	0.045	11/11
1101	0.041	11/11

- From http://pypop.org/popdata/2008/byfreq-DRB1.php.html
  - Table continues for over 60 alleles
  - This locus is FAR from neutral expectations
  - Heterozygote advantage? Difficult to imagine selection this strong!

Underdominance

- Fitness of heterozygote less than either homozygote
- Note that this is not a kind of dominance! (Dominance is about the *phenotype* of the heterozygote; this is about the *fitness*)
- Mainly observed in hybrids–why?

Underdominant math

Helpful to write the fitnesses as:

AA	Aa	aa
1-s	1	1-t

- For underdominance s and t are both negative
- This also has an equilibrium at $p = t/(s+t)$

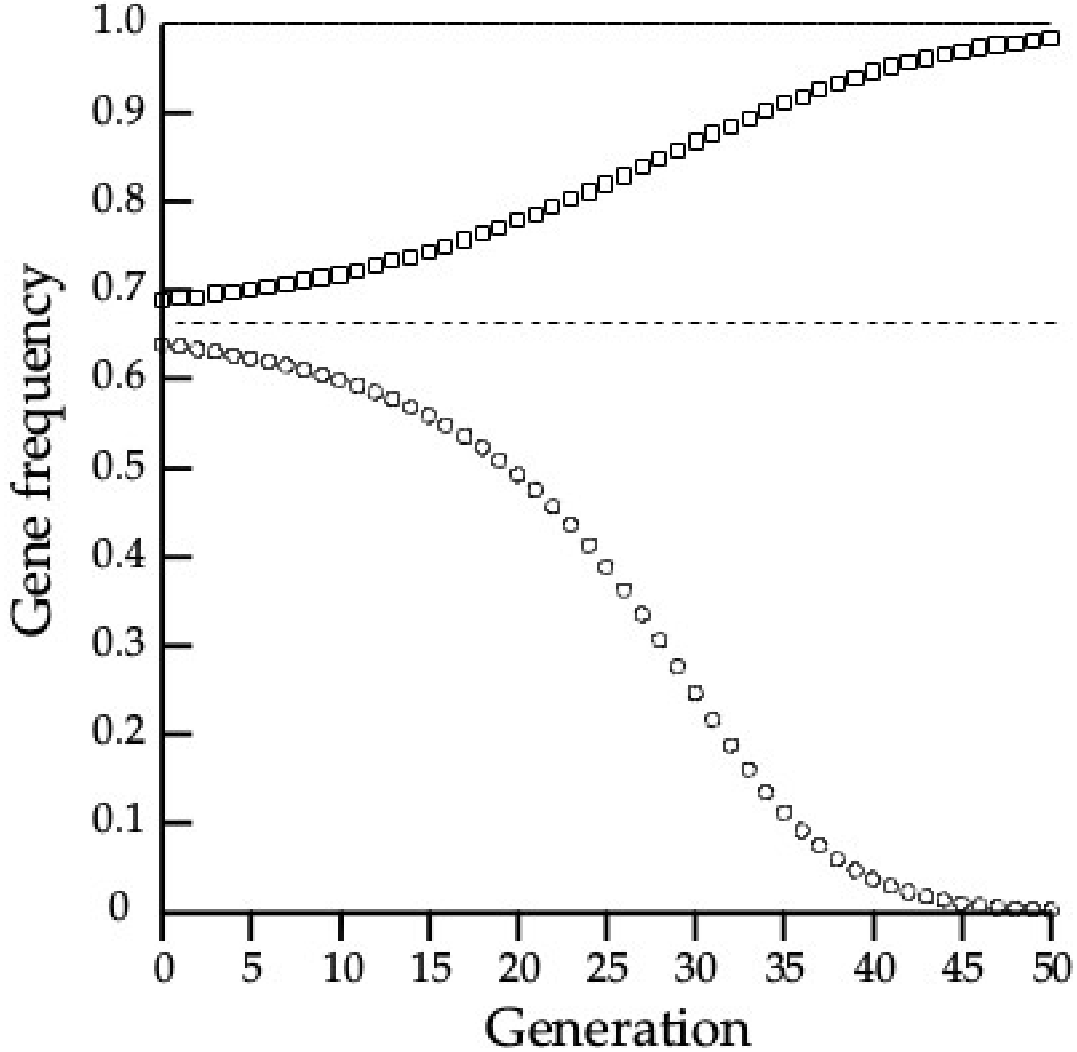
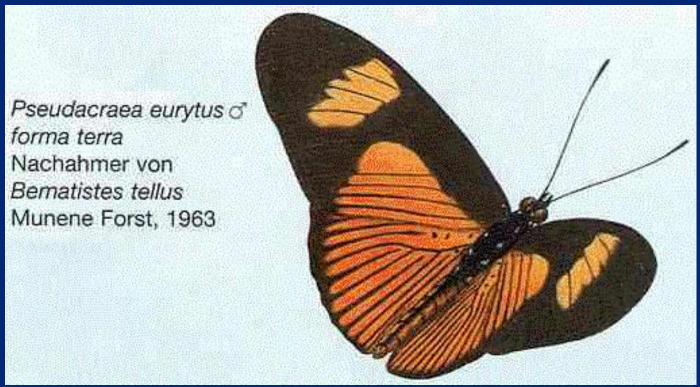


Figure 2.6: Gene frequencies in successive generations when fitnesses of *AA*, *Aa*, and *aa* are underdominant (1.15 : 1 : 1.3) and the initial gene frequency is 0.65 (circles) or 0.68 (squares).

Unstable equilibrium

- Any perturbation (drift, migration, etc) will dislodge the population from the equilibrium and fix one of the alleles
- The less fit allele can fix!
- In a large population, if the allele frequency is on the wrong side of the equilibrium, the less fit allele is favored and will fix deterministically

Failure of evolutionary optimization?



- Blue and orange morphs mimic different inedible species; heterozygote does not successfully mimic anything and is disfavored

- Fitnesses:

BB	BO	OO
1.1	1.0	1.2

- If we introduce 10% orange into a purebred blue population, can it invade?

Local optimization vs. global optimization

- Fitness increases towards the local optimum
- With underdominance, global optimum may not be found
- Drift in a small population could allow either optimum to be found
- Small populations have evolutionary options that large ones do not!

Frequency dependent selection

- The fitness of a phenotype depends on its rarity
  - Rare type has less competition for resources
  - Rare type suffers less from parasites, pathogens, or predators
  - Rare type is sexually attractive
- Often described as equivalent to overdominance (if rare type is favored) or underdominance (if common type is favored)
- This can be true, depending on *how* fitness depends on frequency, but needn't be true

Summary

- When the heterozygote is most fit (overdominance):
  - Population moves to a stable equilibrium
  - At equilibrium, more fit allele is more frequent
- When the heterozygote is less fit (underdominance):
  - Population moves away from an unstable equilibrium point
  - Which allele fixes depends on starting frequencies
  - More fit allele has a larger range in which it will win
- Frequency dependent selection can look like either of these, or do something more complex

Wednesday

No class on Monday: HW due Wednesday

- Natural selection versus drift
- Testing whether a locus is under selection

One-minute responses

- Please:
  - Tear off a slip of paper
  - Give me one comment or question on something that worked, didn't work, needs elaboration, etc.