Lecture 16

Model development
Six Cases: 1 gene, 2 allele model
With exciting real-world examples!
Article 15

Model of Natural Selection

- Allele number passed on is modified by survival and fertility. Assume 'big bang' life history, then

Model of selection

- Likewise,
- We now have the numerator, and continuing in like fashion, we derive the denominator (=all alleles)

Model of Selection

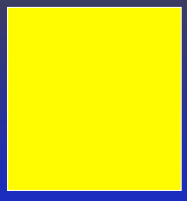
- Yielding,

- To simplify, factor 2 and N_t from the numerator and denominator, and let $l \bullet m = W$ (absolute fitness). We will use relative fitness (w, rather than W), where

Model of Selection

- The selection equation can now be 'iterated' to project future allele frequency change, given initial p, and fitnesses associated with each genotype.

Iteration of the Selection Model



- Selection model is deterministic (unlike drift), predicting specific allele frequency changes

The Selection Equation

$$p_{t+1} = \frac{w_{11}p_t^2 + w_{12}p_t q_t}{w_{11}p_t^2 + 2w_{12}p_t q_t + w_{22}q_t^2}$$

Case	Genotype	Phenotype	Fitness
1	A_1A_1	Purple	1
	A_1A_2	Pink	1
	A_2A_2	White	1

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Case	Genotype	Phenotype	Fitness
1	★A_1A_1	Purple	1
	★A_1A_2	Pink*	1
	★A_2A_2	White	1

*Note; with equal fitnesses, the phenotype of the heterozygote does not matter. The results will be the same

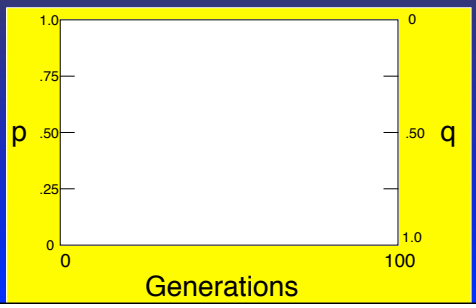
Make a prediction!

Case	Genotype	Phenotype	Fitness
1	★A_1A_1	Purple	1
	★A_1A_2	Pink	1
	★A_2A_2	White	1

(A) p will decrease, resulting in fixation of A_2
(B) p will decrease, and approach 0 asymptotically
(C) p will remain the same
(D) p will increase, approaching 1 asymptotically
(E) p will increase, resulting in fixation of A_1

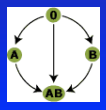
6 'Cases' of Selection

- Case 1: Equal fitnesses ($w_{11}=w_{12}=w_{22}=1$)



Human Example

- Blood groups may be a 'neutral' polymorphism (until transfusion time!)



donors

recipients

Case 2: Selection Against the Dominant Allele

Case	Genotype	Phenotype	Fitness
2	A_1A_1	Purple	$w_{11}=w_{12}<1$
	A_1A_2	Purple	$w_{12}=w_{11}<1$
	A_2A_2	White	1

- A new way to express the strength of selection:

s=the selection coefficient

Case 2: Selection against dominant What will happen?

Case	Genotype	Phenotype	Fitness
2	A_1A_1	Purple	$w_{11}=w_{12}<1$
	A_1A_2	Purple	$w_{12}=w_{11}<1$
	A_2A_2	White	1

(A) p will decrease, resulting in fixation of A_2
(B) p will decrease, and approach 0 asymptotically
(C) p will reach an equilibrium between 0 and 1
(D) p will increase, approaching 1 asymptotically
(E) p will increase, resulting in fixation of A_1

How do we determine the outcome?

- Which allele will increase?
- How 'exposed' is the allele that is declining?

Human Example

- Huntington's Disease - dominant gene causes gradual disruption of nerve function
- Why is it still around? Mutation. Effects occur after most reproduction.
- High frequency near Lake Maracaibo; founder effect traced to one early immigrant who bore 10 children!
- http://evolution.berkeley.edu/evolibrary/article/0_0_0/medicine_05

Case 3 - Selection Against the Recessive

Case	Genotype	Phenotype	Fitness	Selection coefficient
3	A_1A_1		1	0
	A_1A_2		1	0
	A_2A_2	★ White	$w_{22}<1$	s_{22}

Case 3 – Selection against the recessive. Make a prediction!

Case	Genotype	Phenotype	Fitness	Selection coefficient
3	A_1A_1		1	0
	A_1A_2		1	0
	A_2A_2	★ White	$w_{22}<1$	s_{22}

(A) p will decrease, resulting in fixation of A_2
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(D) p will increase, approaching 1 asymptotically
(E) p will increase, resulting in fixation of A_1

Human Example

- Cystic fibrosis (recessive allele in CF gene); most common lethal genetic disease of European and European derived populations!
- Blockages in sweat and mucus glands; leads to respiratory failure, etc.
- May be still around because (1) recessive lethals are difficult to get rid of when in low proportions, and (2) in the past, the homozygotes may have had an advantage in defense against tuberculosis!
- Read more: http://www.nhlbi.nih.gov/health/dci/Diseases/cf/cf_what.html

Case 4: No dominance - linear arrangement of fitnesses

Case	Genotype	Phenotype	Fitness	Selection coefficient
4	A_1A_1	Purple	$w_{11}<w_{12}$	$s_{11}>s_{12}$
	A_1A_2	Pink	$w_{12}<1$	s_{12}
	A_2A_2	White	1	0

Case 4 - No dominance Make a prediction!

Case	Genotype	Phenotype	Fitness	Selection coefficient
4	A_1A_1	Purple	$w_{11}<w_{12}$	$s_{11}>s_{12}$
	A_1A_2	Pink	$w_{12}<1$	s_{12}
	A_2A_2	White	1	0

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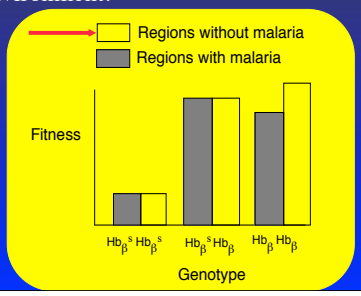
Human Example

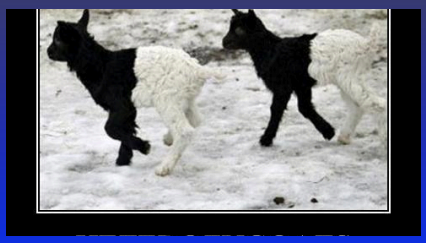
- Sickle cell anemia in a non-malarial environment.



Case 5 - Heterozygote superiority

Case	Genotype	Phenotype	Fitness	Selection coefficient
5	A_1A_1	Purple	w_{11}	s_{11}
	A_1A_2	Pink	1	0
	A_2A_2	White	w_{22}	s_{22}

Heterozygoat superiority…



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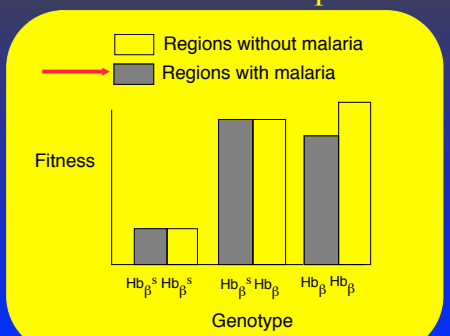
Case 5 - Heterozygote superiority

- With heterozygote superiority, what is the eventual equilibrium p?

Human Example



Case 6 - Heterozygote inferiority

- $W_{11}=1+s_{11}$
- $W_{12}=1$
- $W_{22}=1+s_{22}$
- s is a selective 'favor' coefficient (for this case only) because….

Case 6 - Heterozygote Inferiority

Case	Genotype	Phenotype	Fitness	Selection coefficient*
4	A_1A_1	Purple	1 or W_{11}	$1+s_{11}$
	A_1A_2	Pink	$W_{12}<1$ (lowest)	1
	A_2A_2	White	1 or W_{22}	$1+s_{22}$

Note: s is a selection 'favor' coefficient in this case only…

Case 6 - Heterozygote inferiority

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4	A_1A_1	Purple	1 or W_{11}	$1+s_{11}$
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Case 6 - Heterozygote inferiority

- What is the eventual fate of alleles A_1 and A_2?

Be Able to Answer These Questions!

- When (what case?) is the disfavored allele eliminated?
- When does the disfavored allele persist in low frequencies?
- When is allelic diversity preserved?
- When does initial p, q matter?

Real world selection

- Does evolution follow the pattern predicted by the selection equation in the real world?
- Most famous example: *Biston betularia* - peppered moth, of Britain, studied by H. B. D. Kettlewell.

Genetics of Melanism

- One gene, two alleles. M dominant over m. M produces dark pigmentation in dominant homozygote and heterozygote.
- MM=melanic
- Mm=melanic
- mm=typical

Demonstration of Selection

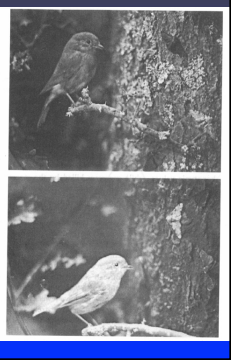
- Clarke and Sheppard (1966) experiment

Phenotype:	Melanic		Typical	
Environment	Exposed	Survived	Exposed	Survived
Dark Background	70	58	70	39
Pale Background	40	24	40	32

Biston betularia

- Which case of selection is this?

(A) Selection against the dominant
(B) Selection against the recessive
(C) Heterozygote superiority
(D) Heterozygote inferiority



Biston betularia

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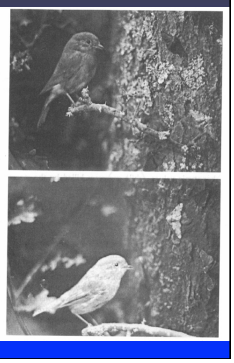

Contrasting Patterns of Selection

- Selection acts in opposite directions in the two environments.

Summary

- In a one-gene, two allele system, there are 6 'cases' of selection
- Most cases of selection result in elimination of disfavored alleles
- Deleterious recessive alleles are difficult to remove *via* selection
- Heterozygote superiority maintains genetic diversity at a locus by favoring individuals that contain both alleles