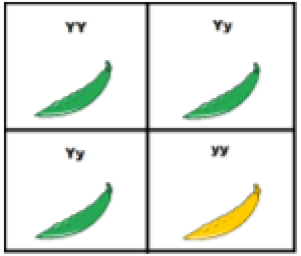
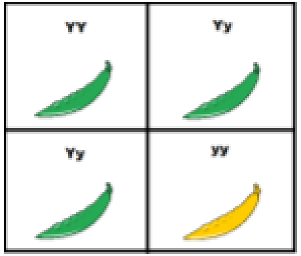
NATURAL SELECTION: Types at single loci

Duke UNIVERSITY



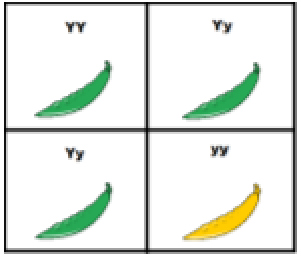
Selection and dominance

- In previous example, all adult “aa” die
  - w (MM) = 1.00 w (MN) = 1.00 w (NN) = 0
  - Which allele is dominant/ recessive?



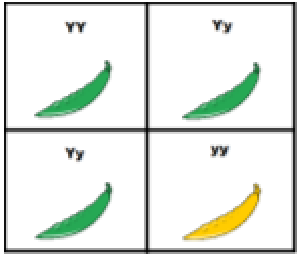
Selection and dominance

- In previous example, all adult "aa" die
  - w (MM) = 1.00 w (MN) = 1.00 w (NN) = 0
  - N is **recessive** to M, and N is detrimental (bad)
- A different example:
  - w (MM) = 1.00 w (MN) = 0 w (NN) = 0
  - What will this selection do differently?
  - Which allele is dominant?



Selection and dominance

- In previous example, all adult "aa" die
  - w (MM) = 1.00 w (MN) = 1.00 w (NN) = 0
  - N is recessive to M, and N is detrimental (bad)
- A different example:
  - w (MM) = 1.00 w (MN) = 0 w (NN) = 0
  - N is **dominant** to M, and N is detrimental (bad)
    - With dominant detrimental, heterozygotes respond to selection
- A third example:
  - w (MM) = 1.00 w (MN) = 0.5 w (NN) = 0



Selection and dominance

- In previous example, all adult “aa” die
  - w (MM) = 1.00 w (MN) = 1.00 w (NN) = 0
  - N is recessive to M, and N is detrimental (bad)

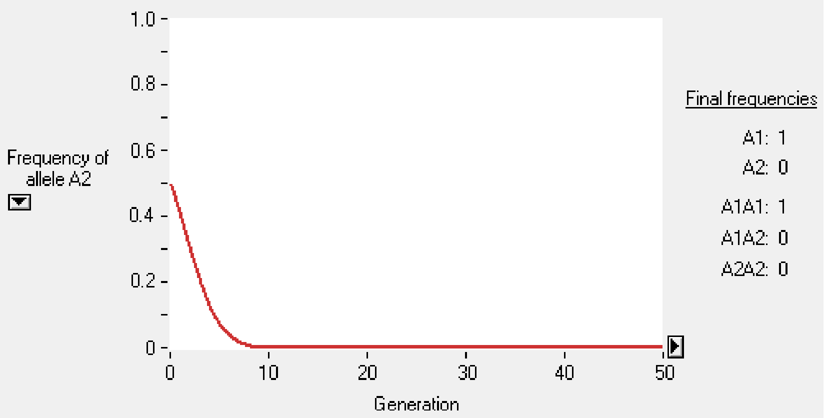
- A different example:
  - w (MM) = 1.00 w (MN) = 0 w (NN) = 0
  - N is dominant to M, and N is detrimental (bad)
    - With dominant detrimental, heterozygotes respond to selection

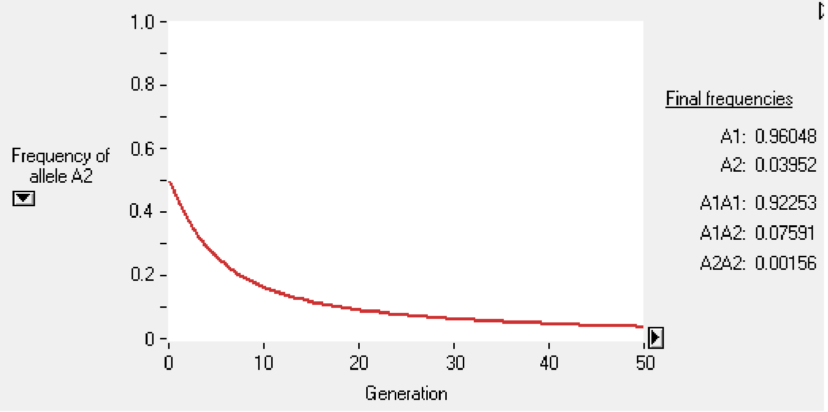
- A third example: “**no dominance**”
  - w (MM) = 1.00 w (MN) = 0.5 w (NN) = 0

Effect of dominance with directional selection

- **Dominant detrimental**
  - w(A1A1) = 1.0
  - w(A1A2) = 0.5
  - w(A2A2) = 0.5

- **Recessive detrimental**
  - w(A1A1) = 1.0
  - w(A1A2) = 1.0
  - w(A2A2) = 0.5





Effect of dominance with directional selection

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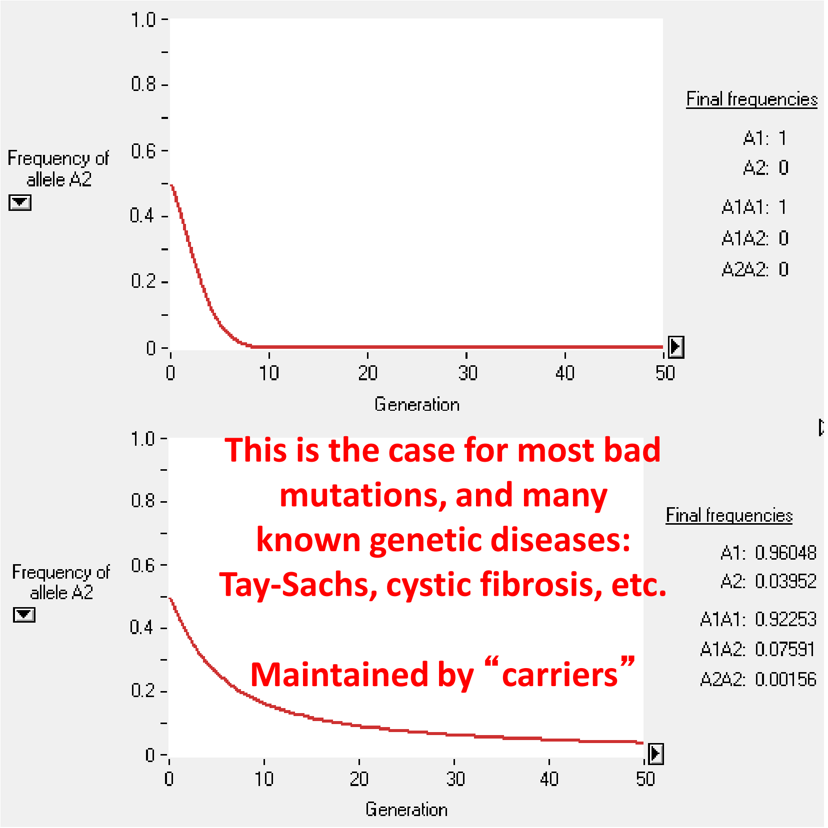
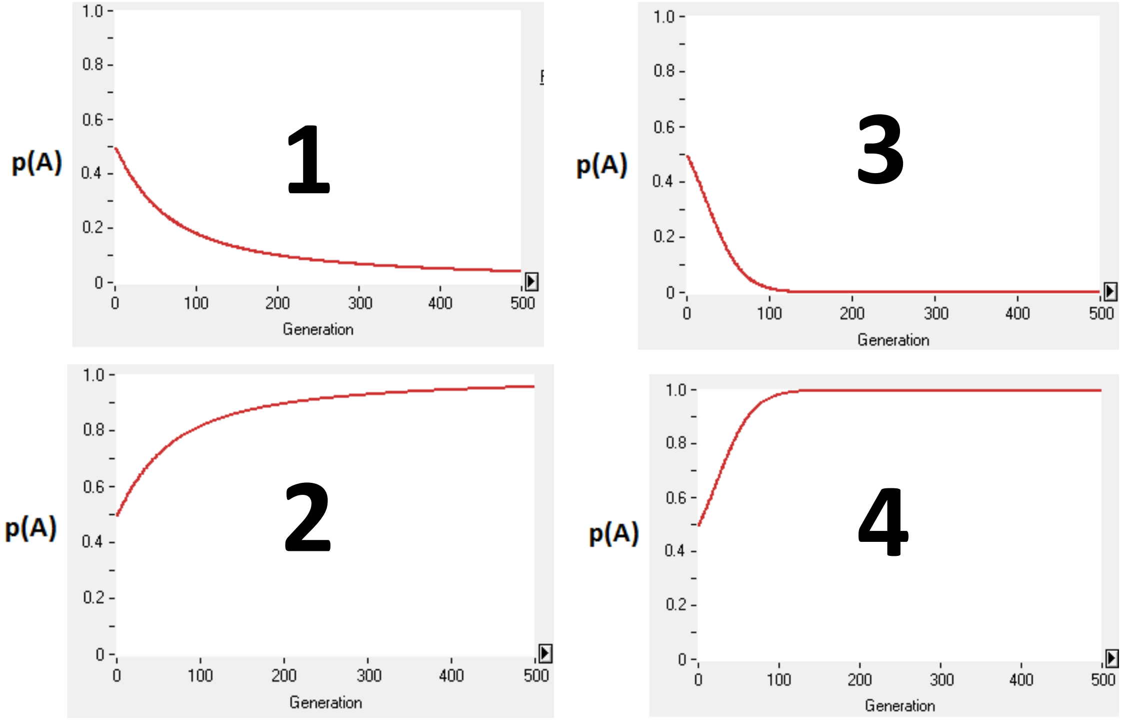


Which depicts the frequency change in the lactose intolerance allele (A) by selection?

AA: 0.95 Aa: 1.00 aa: 1.00

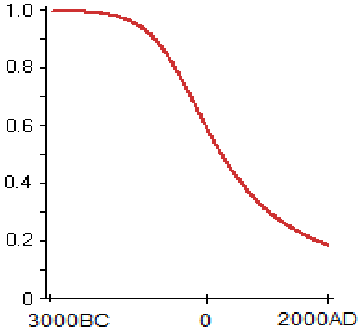


Types of selection on single locus: 1) Directional selection

- **Directional selection**
  - One allele *eventually* replaces the other
    - w (AA) = 1.00 w (Aa) = 1.00 w (aa) = 0
    - w (AA) = 1.00 w (Aa) = 0.5 w (aa) = 0
    - w (AA) = 0.1 w (Aa) = 0.2 w (aa) = 1.00
    - Lactase: w (AA) = 0.95 w (Aa) = 1.00 w (aa) = 1.00
  - w (AA) ≤ w (Aa) ≤ w (aa) OR
  - w (AA) ≥ w (Aa) ≥ w (aa)

Lactose intolerance allele

p (A)

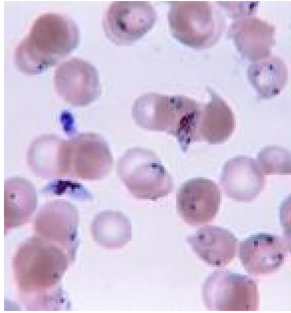


Types of selection on single locus: 2) Heterozygote advantage

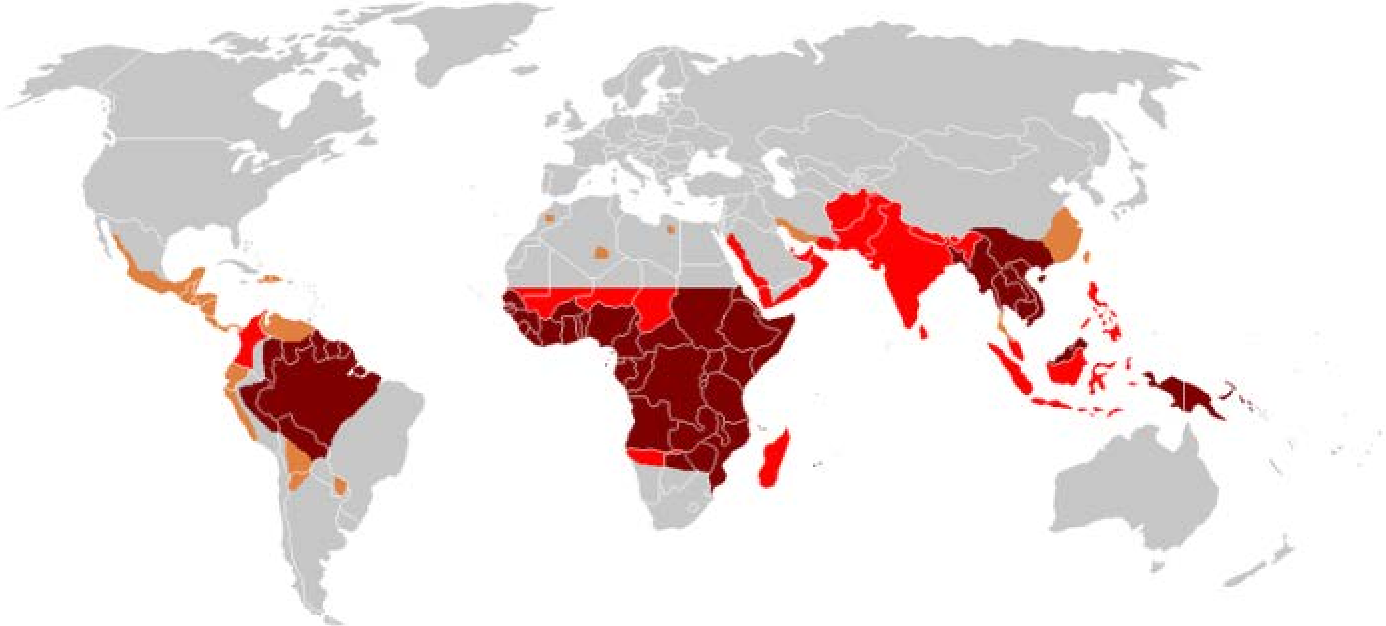
- Also called “overdominance”
  - Most fit genotype is the heterozygote (Aa)
    - w (AA) = 0.85 w (Aa) = 1.0 w (aa) = 0.05

- One allele **does not** replace the other
  - Example: Sickle cell anemia and malaria resistance

Malaria incidence



- ~4% chance of death by malaria in sub-Saharan Africa
  - Mosquito bite transmits Plasmodium protozoa



Sickle Cell Anemia

- Recessive genetic disease (aa)
  - Sickle cells die faster than normal RBCs
  - Sickle cells deliver less oxygen to cells
  - Symptoms: chronic pain & fatigue

- If heterozygote (Aa)
  - Called "Sickle cell trait"
  - Usually OK, but cells may sickle during intense physical exertion

Intersection: Sickle Cell & Malaria

- Individuals heterozygous for sickle cell (Aa) are (more) resistant to malaria!
  - *Old thought*: Invasion, growth, & development of Plasmodium may be reduced in blood cells in Aa?
  - *Recent*: Aa more tolerant to sickle cell symptoms but retain same infection load?
  - *Recent2*: Infected Aa cells more likely to be eliminated by spleen since being Aa prevents one defense of Plasmodium

Ferreira et al (2011) *Cell* 145: 398-409
Cyrklaff et al (2011) *Science* 334:1283-6

Sickle Cell Exhibits Heterozygote Advantage *in Some Populations*

Subsaharan Africa	Sample Fitness
AA – Susceptible to malaria	w(AA) = 0.85
Aa – Generally fine!	w(Aa) = 1.00
aa – Sickle cell anemia disease	w(aa) = 0.05

Fate of new “a”
mutation in
“A” population:

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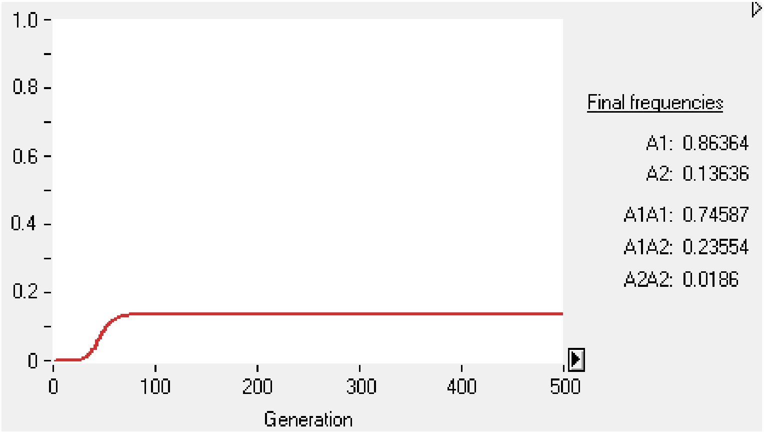
Fate of new "a" mutation in "A" population:

q (a)



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Fate of new "a" mutation in "A" population:

Predictable:

$$q(a) = \frac{1-w(AA)}{(1-w(aa)) + (1-(w(AA))}$$

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Fate of new "a" mutation in "A" population:

Predictable:

$$q\,(a) = \frac{1-0.85}{(1-0.05) + (1-0.85)}$$

Sickle Cell Exhibits Heterozygote Advantage *in Some Populations*

Subsaharan Africa	Sample Fitness
AA – Susceptible to malaria	w(AA) = 0.85
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aa – Sickle cell anemia disease	w(aa) = 0.05

Fate of new “a” mutation in “A” population:

Predictable:

$$q(a) = \frac{0.15}{0.95 + 0.15} = 0.136$$

Sickle Cell Exhibits Heterozygote Advantage *in Some Populations*

Subsaharan Africa	Sample Fitness
AA – Susceptible to malaria	w(AA) = 0.85
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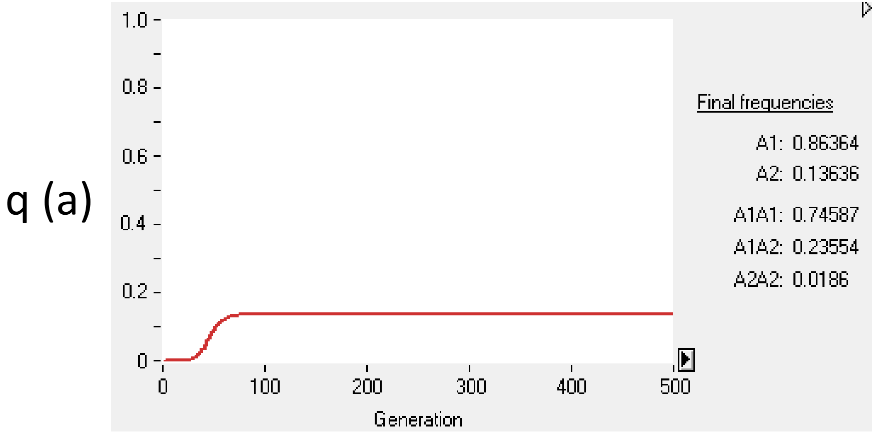
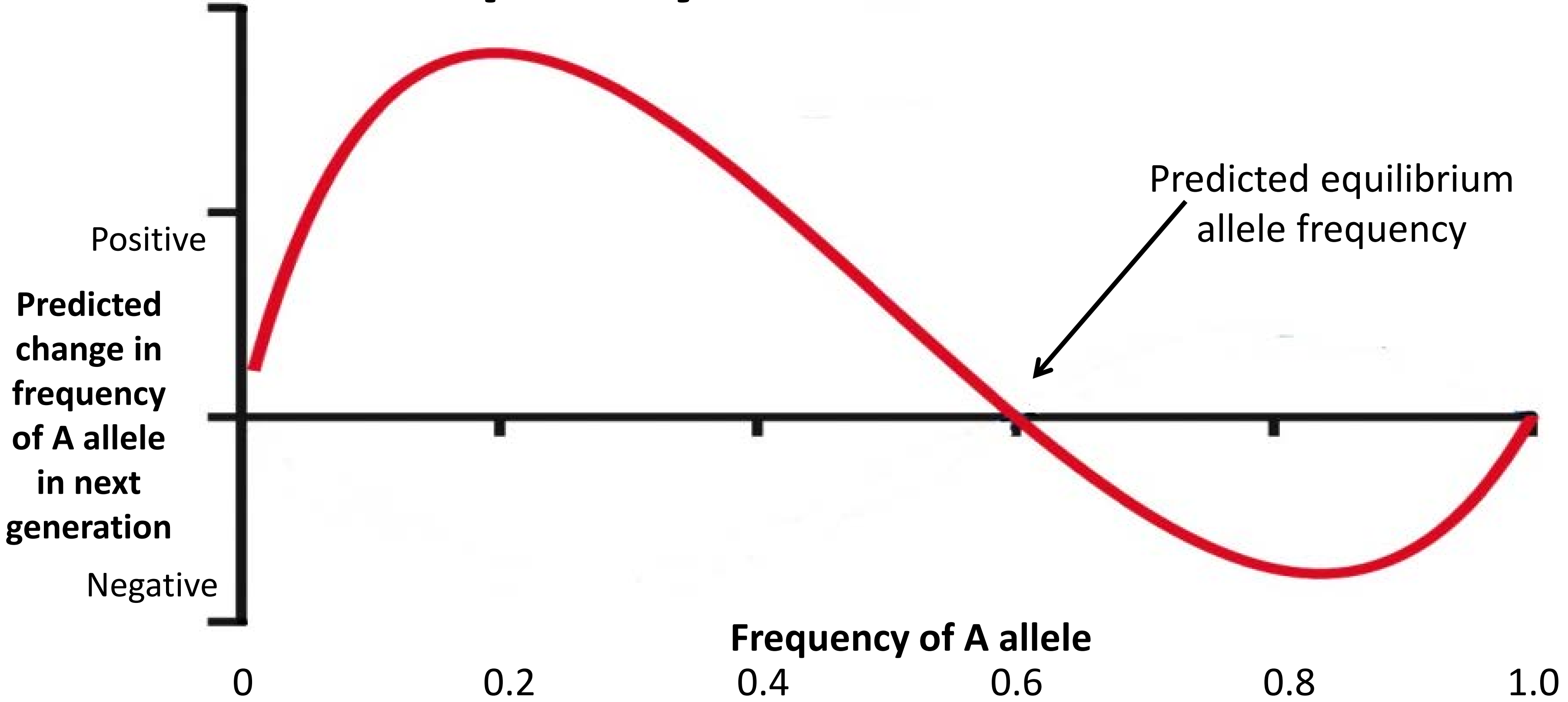
Fate of new “a” mutation in “A” population:



Types of selection on single locus: 2) Heterozygote advantage

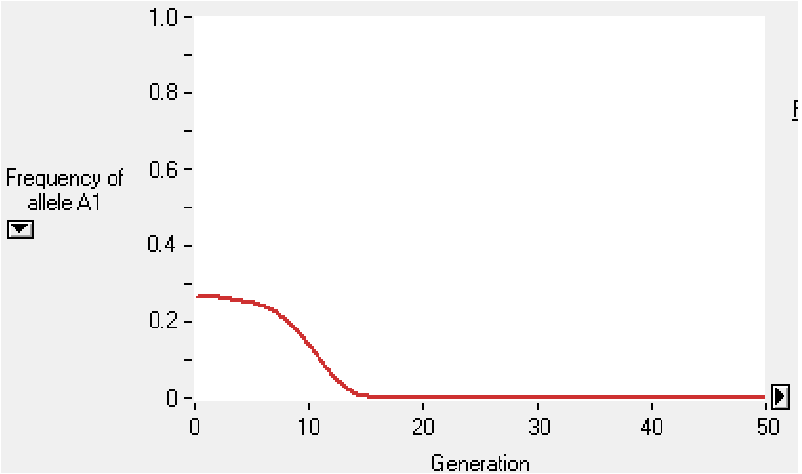
- Also called "overdominance"
  - Most fit genotype is the heterozygote (Aa)
    - w (AA) = 0.85 w (Aa) = 1.0 w (aa) = 0.05
  - Leads to a "stable equilibrium"
    - Both alleles retained in the population
    - Alleles go to "equilibrium" frequencies
    - If not at equilibrium frequency, move back to it

Graphical representation of changes in allele frequency with overdominance



Types of selection on single locus: 3) Heterozygote disadvantage

- Also called "underdominance"
  - LEAST fit genotype is the heterozygote (Aa)
    - w (AA) = 1.00   w (Aa) = 0.2   w (aa) = 0.5
  - Leads to a "**unstable** equilibrium" (0.272727)
    - If start **below** equilibrium, go to loss
      - Starting p(A1) = 0.27

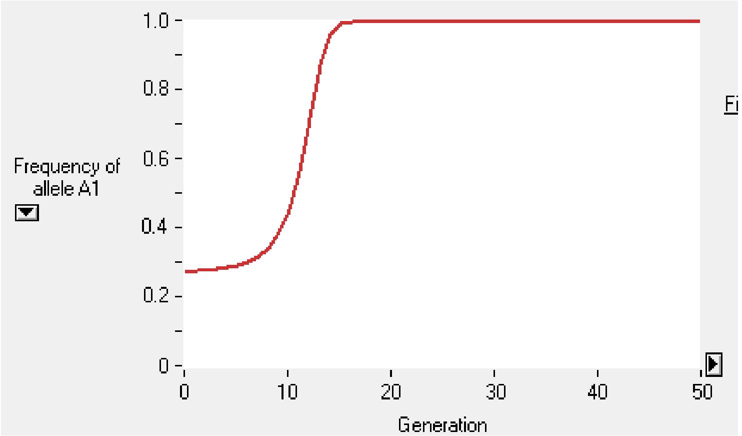


Types of selection on single locus: 3) Heterozygote disadvantage

- Also called “underdominance”
  - LEAST fit genotype is the heterozygote (Aa)
    - w (AA) = 1.00 w (Aa) = 0.2 w (aa) = 0.5
  - Leads to a “**unstable** equilibrium” (0.272727)

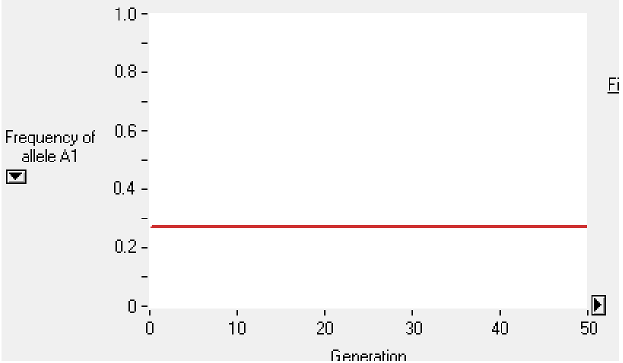
    If start below equilibrium, go to loss

    If start **__above__** equilibrium, go to fixation
    - Starting p(A1) = 0.275

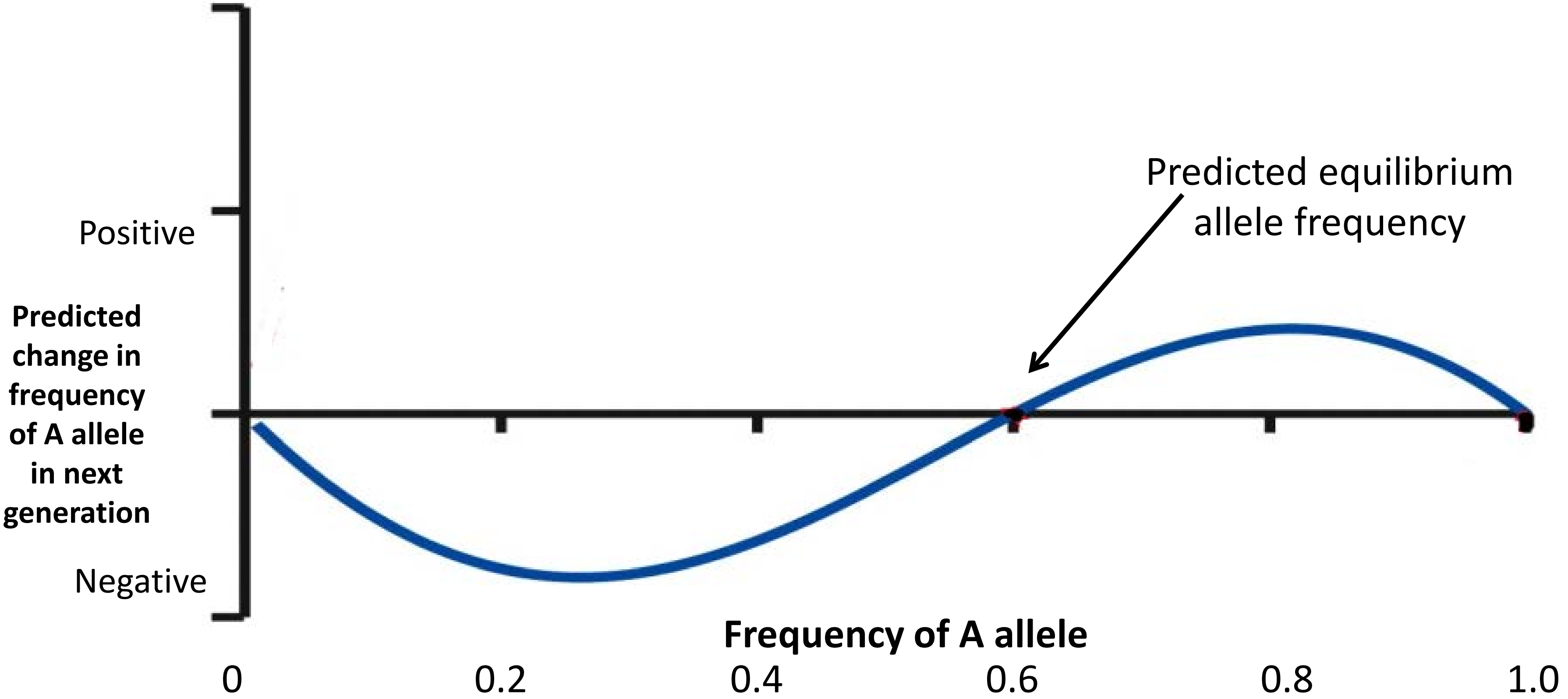


Types of selection on single locus: 3) Heterozygote disadvantage

- Also called "underdominance"
  - LEAST fit genotype is the heterozygote (Aa)
    - w (AA) = 1.00   w (Aa) = 0.2   w (aa) = 0.5
  - Leads to a "**unstable** equilibrium" (0.272727)
    - If start below equilibrium, go to loss
    - If start above equilibrium, go to fixation
    - If start (and STAY) <u>**at**</u> equilibrium, alleles persist
      - But very unlikely to stay...



Graphical representation of changes in allele frequency with underdominance



Types of selection on single locus: 4) Frequency dependent selection

- Previous examples assumed fitness was independent of the rest of the population

- Sometimes, it’s better to be “rare”...
- But being “better” makes you become more common
- Leads to equilibrium:
  - Negative frequency dependent selection

Example: Sex Ratio

- In many species, sex (male vs. female) determined genetically
  - In mammals, XX vs. XY, so mostly locked in to 50-50 sex ratio by transmission
  - In other species, alleles at a gene cause individual to become male vs. female

- If females are ***rare***, is it better to produce male or female offspring?
  - Would selection favor "male" or "female" allele?

Example: Sex Ratio

- Computer science club marooned on an island
  - What is likely fitness of average guy on island?
  - What is likely fitness of the one female?

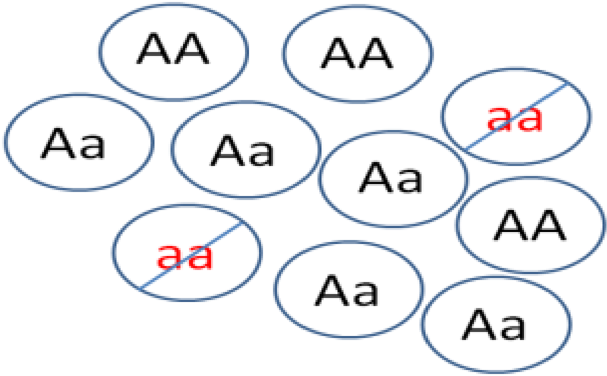
Outcome of Negative Frequency Dependent Selection

- When rare, allele has advantage
- When common, allele has disadvantage
- **Genetic variation maintained in population!**
- If have 2 alleles, what do you predict the "equilibrium allele frequency" to be?

- What if a third allele is introduced into the population?

Single locus selection discussed

- Directional selection favoring one allele
  - Effects of dominance
- Heterozygote advantage
- Heterozygote disadvantage
- Frequency dependent selection



- All affect genotype & allele frequencies, but act on *phenotype*

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