Genome 371, 12 March 2010, Lecture 16

Human Origins, Migrations, & Race

- Final exam: Monday, 8:30 am, Hogness (start at 8 am if you want extra time)

  http://www.washington.edu/home/maps/

- Bring a calculator!

- Covers: Primary emphasis on material since exam 2

  lectures 13, 14, 15, 16

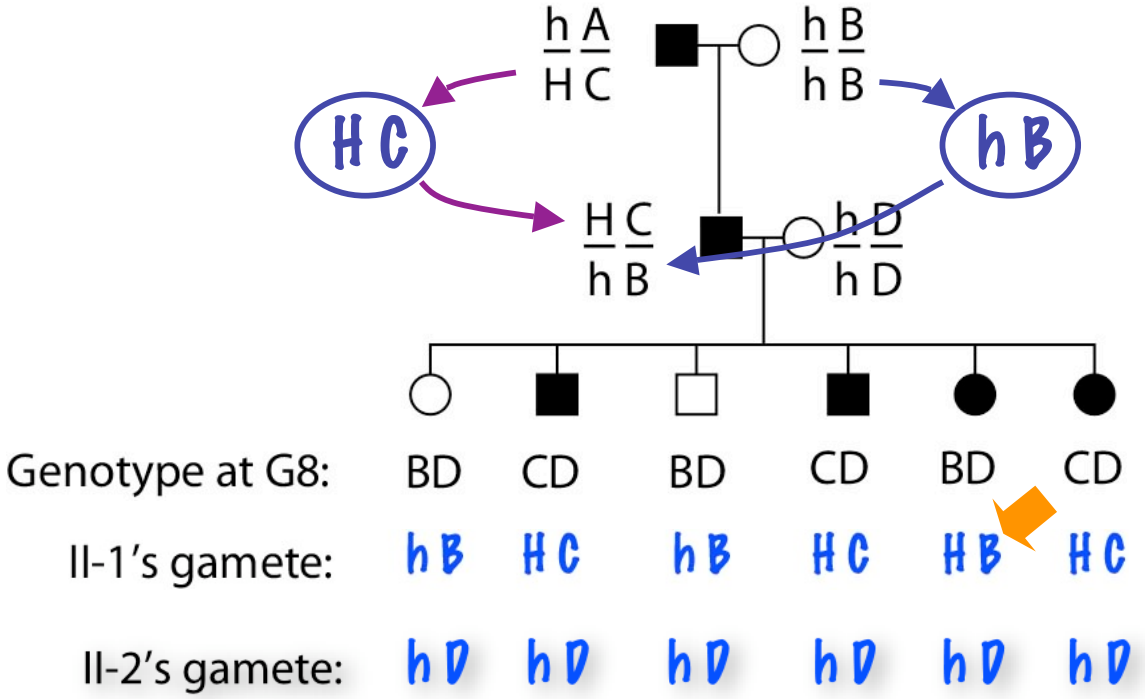
- Questions

LOD Score Digression…

1. Figure out the phase in II-1

   what are the parental types

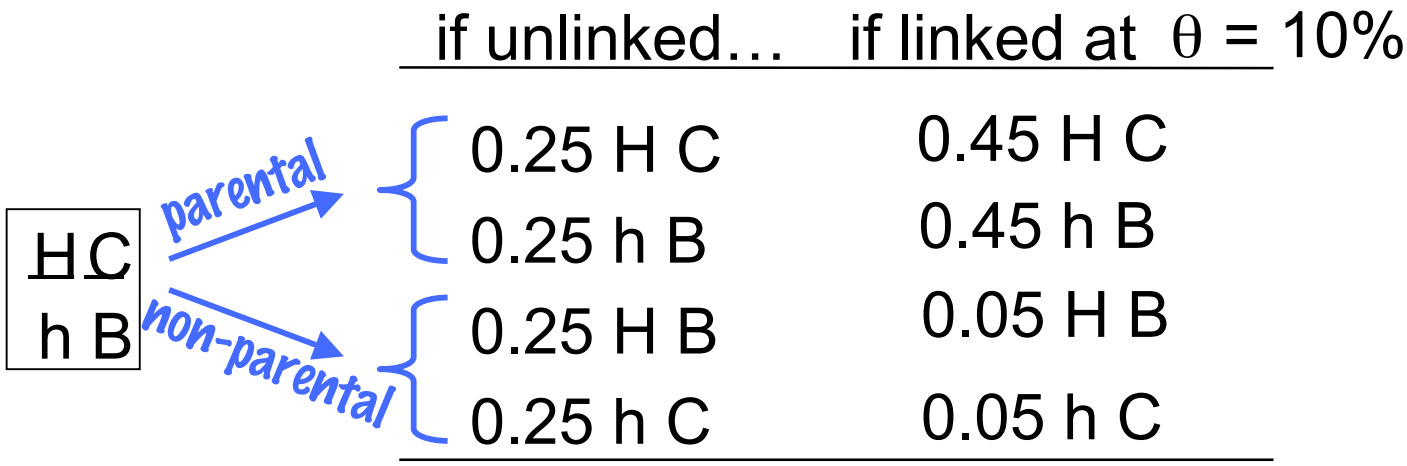
2. Figure out the gametes produced by II-1



Previously calculated LOD score for θ = 5%

Let's redo LOD score calculation for θ = 10%

Possible gametes from II-1:



Probability of the observed genotype if H/h and G8 loci are…

	unlinked	linked @ θ = 10%
Child #1 h B/h D	0.25 x 1 = 0.25	0.45 x 1 = 0.45
Child #2 H C/h D	0.25 x 1 = 0.25	0.45 x 1 = 0.45
Child #3 h B/h D	0.25 x 1 = 0.25	0.45 x 1 = 0.45
Child #4 H C/h D	0.25 x 1 = 0.25	0.45 x 1 = 0.45
Child #5 H B/h D	0.25 x 1 = 0.25	0.05 x 1 = 0.05
Child #6 H C/h D	0.25 x 1 = 0.25	0.45 x 1 = 0.45

II-1's gametes:

Parental = HC, hB

$$LOD_{\theta=10\%} =$$

$$\log_{10}\left[\frac{\text{probability of observed genotypes if the loci are linked at 10 cM}}{\text{probability of observed genotypes if the loci are unlinked}}\right]$$

$$\log_{10}\left[\frac{0.45^5 \times 0.05}{0.25^6}\right]$$

$$= 0.878$$

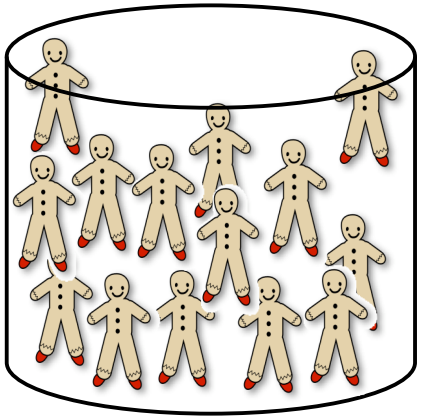
Studying the genetics of populations

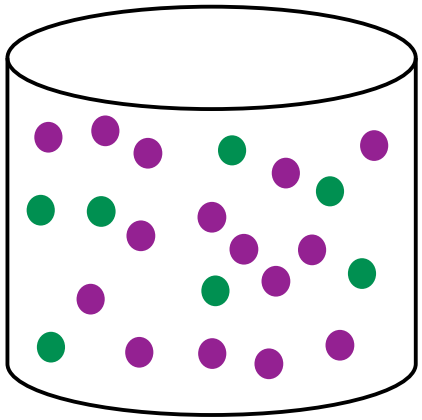
Essential concept: Gene pool

"Collection" of all alleles of all individuals in a population

Within a gene pool, alleles have frequencies

Allele frequency = proportion of an allele among all alleles of a given gene





Hardy-Weinberg Equilibrium (HWE)

- Should be familiar
- Brief review: SNP with two alleles A and a

  Frequency A = p

  Frequency a = q

  $p + q = 1$

- If certain assumptions hold:

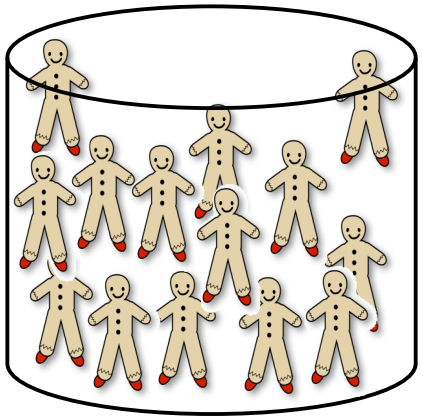
  Frequency AA = p^2

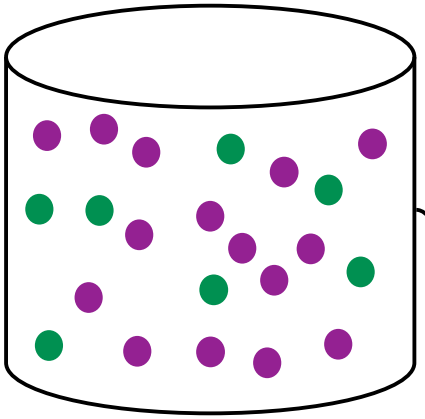
  Frequency Aa = $2pq$

  Frequency aa = q^2

  $p^2 + 2pq + q^2 = 1$

How does HWE arise?





Frequency A = p

Frequency a = q

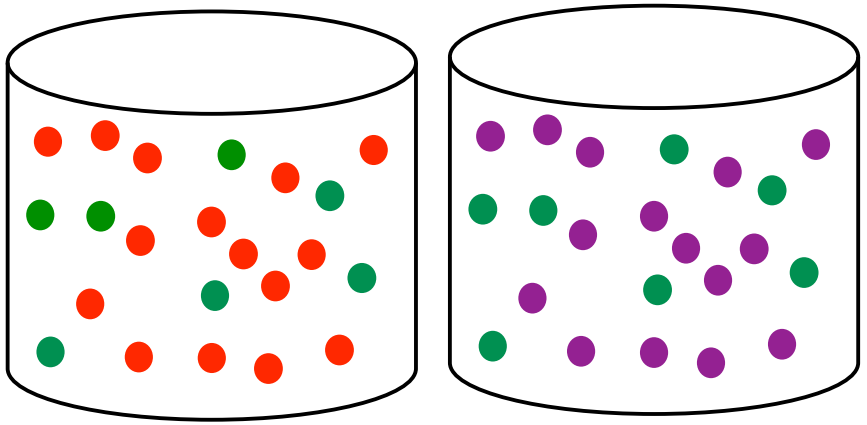
Possible gametes

sperm

egg	p	q
p	p^2	pq
q	pq	q^2

HWE is useful! Example 1

Color blindness is an X-linked recessive trait. If the frequency of the color blindness allele is q, what fraction of males and females in the population are expected to be colorblind?



Males: q

Females: q^2

If q = 0.01

Males: 0.01

Females: 0.0001

HWE is useful! Example 2

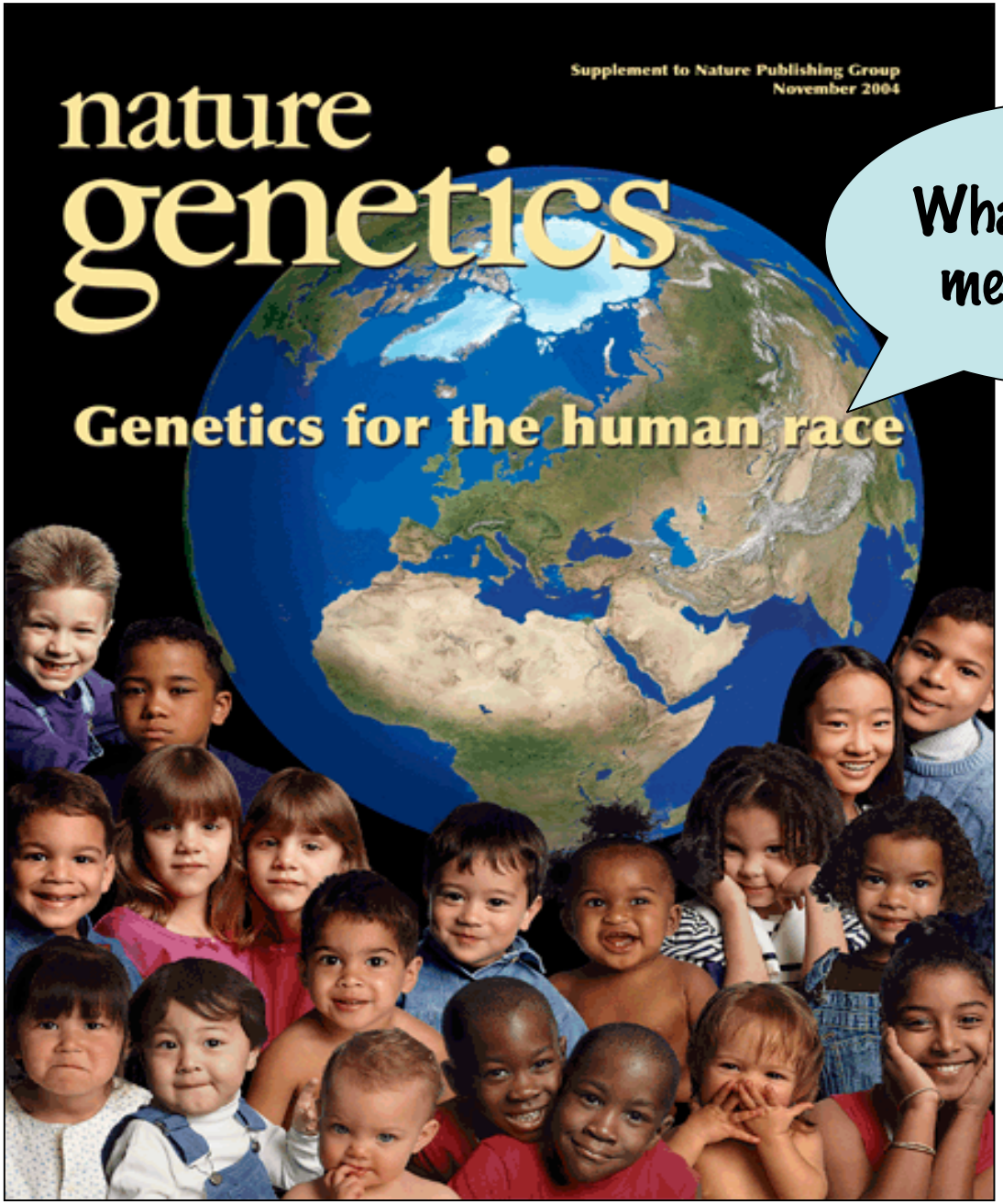
One of the motivations of eugenics (the horribly flawed idea of selective breeding in humans) was to eliminate rare diseases from the population. Using the principle of HWE show why this is not a practical goal.

Because most rare alleles are “hidden” in heterozygote genotypes

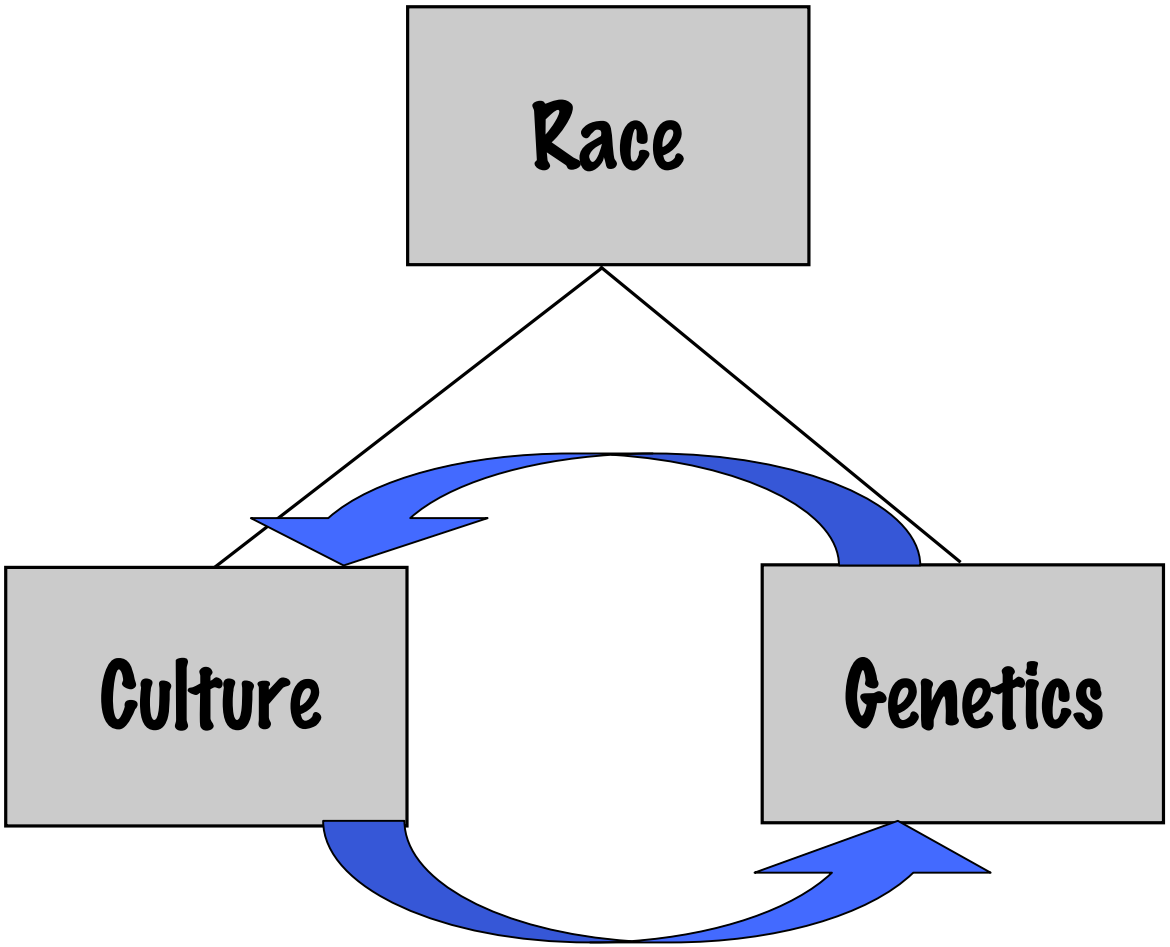
If $q = 0.001$ then:

$q^2 = 0.000001$

$2pq = 0.002$

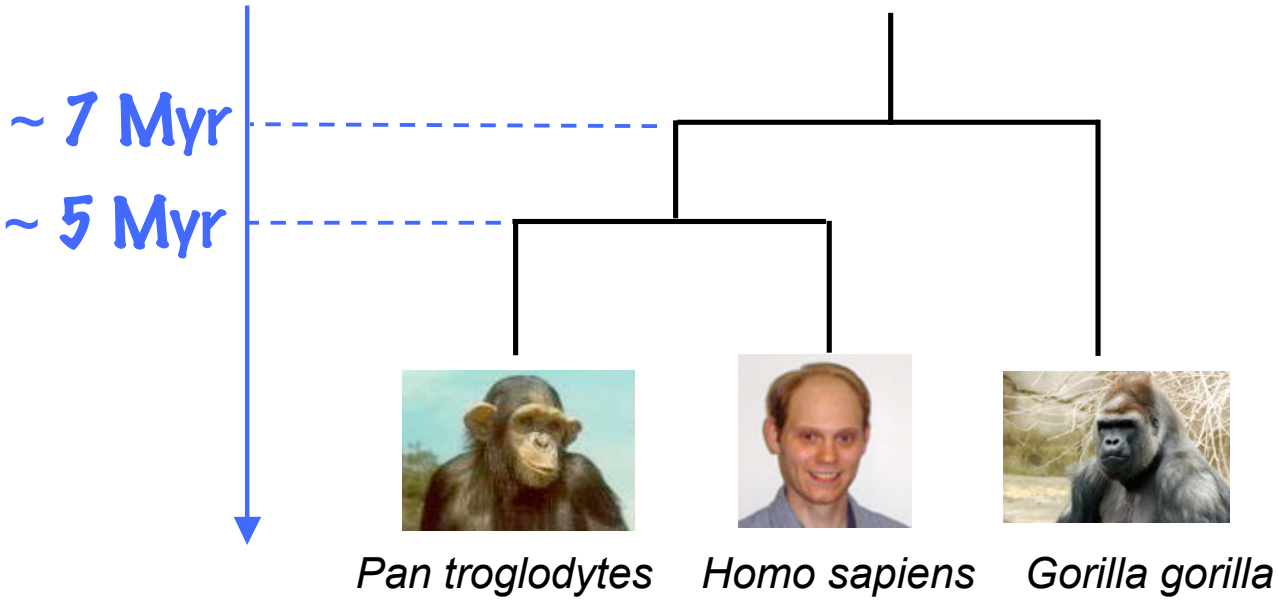

Supplement to Nature Publishing Group
November 2004
nature
genetics
Genetics for the human race
What does race mean to you?

“Race” is Complex



Who Are Our Closest Living Relatives?

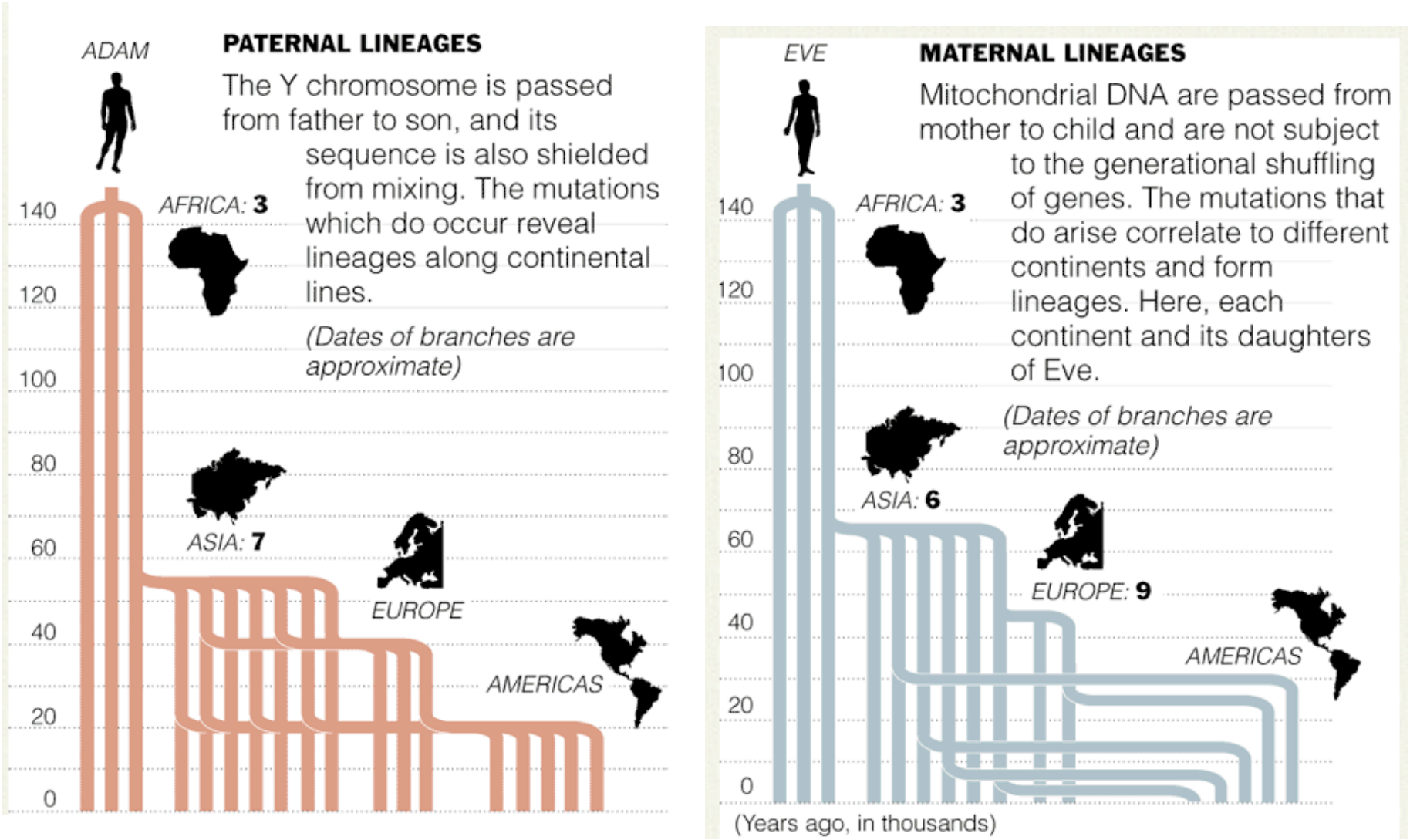
How would you study the relationship of different species?



How do you think these dates are estimated?

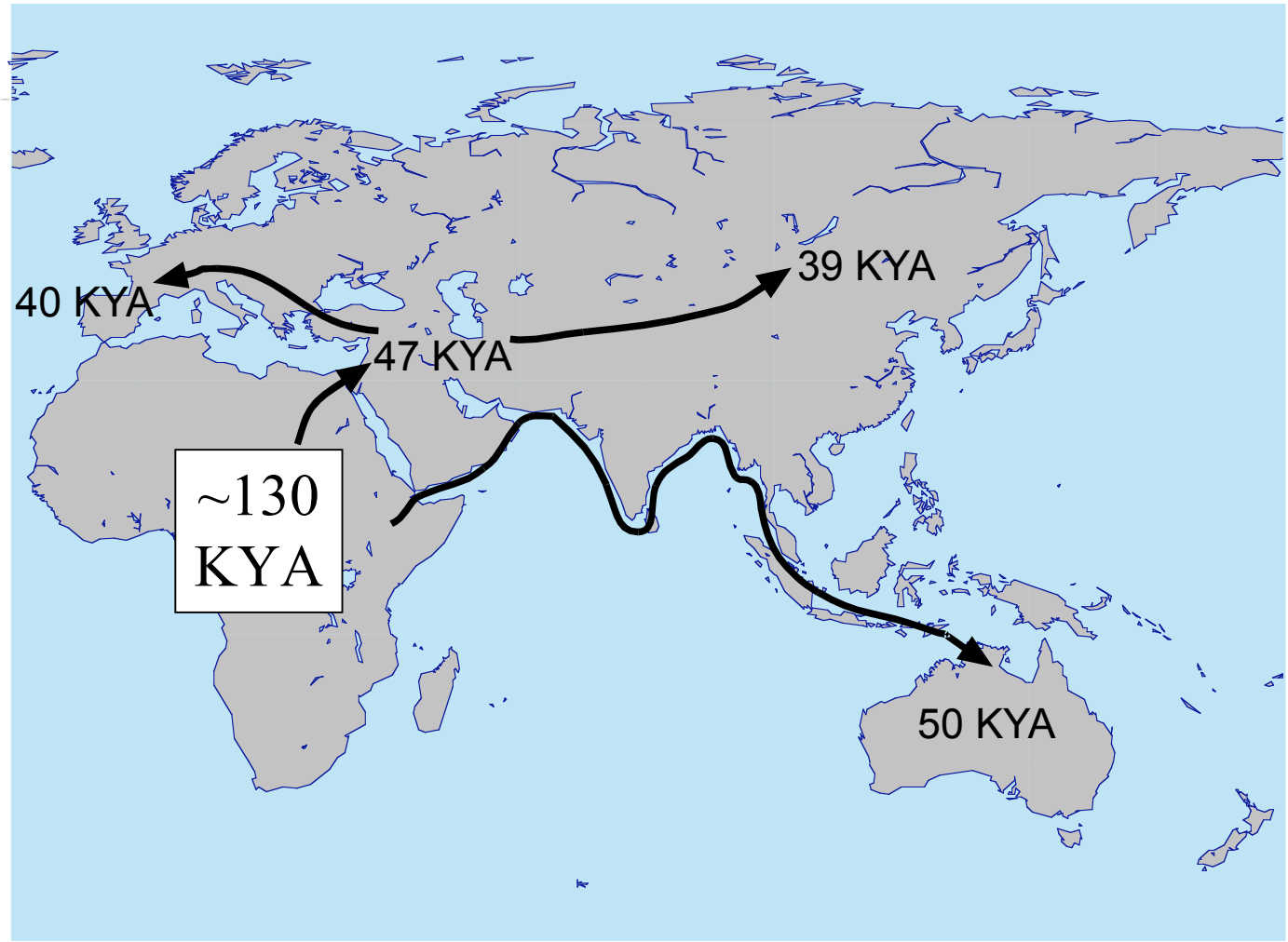
Misconception 1: Humans evolved from chimps

Inferring Human Evolutionary History



Misconception 2: Mitochondrial Eve was the only female alive

Human Migrations and “Out of Africa”



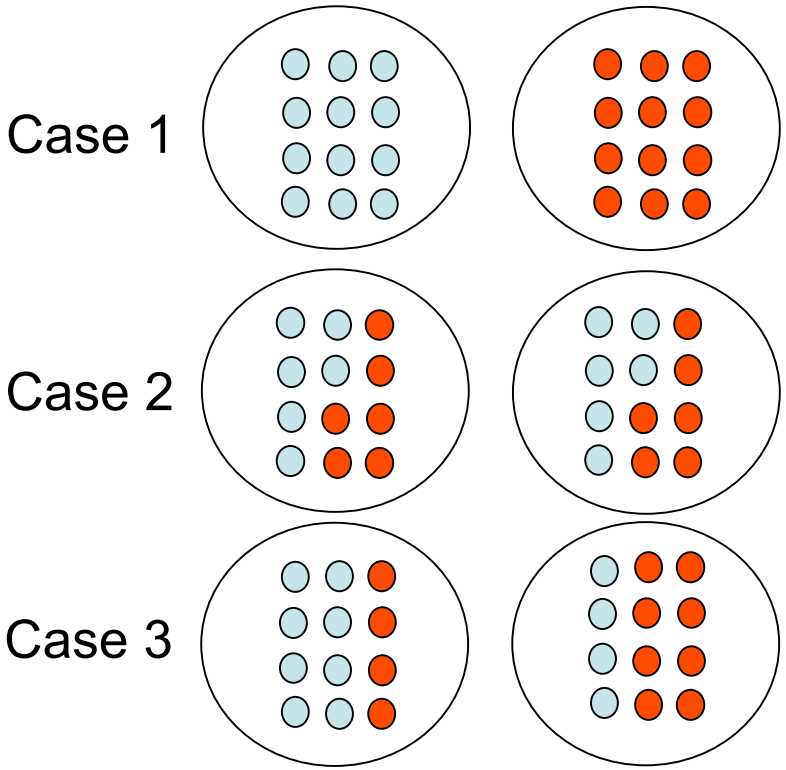
How Different Are Human Populations From One Another?

- How much population genetic structure exists in humans?

Unstructured Structured

- How do we quantify population structure?
  - F_{ST}
  - Measures the allele frequency difference between populations
  - Varies between 0 and 1 [or equivalently between 0% and 100%]
  - Partitions genetic variation into within and between population components

Understanding F_{ST}



	Variation between populations	Variation within populations
Case 1	100 %	0 %
Case 2	0 %	100 %
Case 3	11 %	89 %

F_{ST} in humans is ~0.10; What does this mean?

Why Do Allele Frequencies Vary Between Populations?

- Because of our evolutionary history

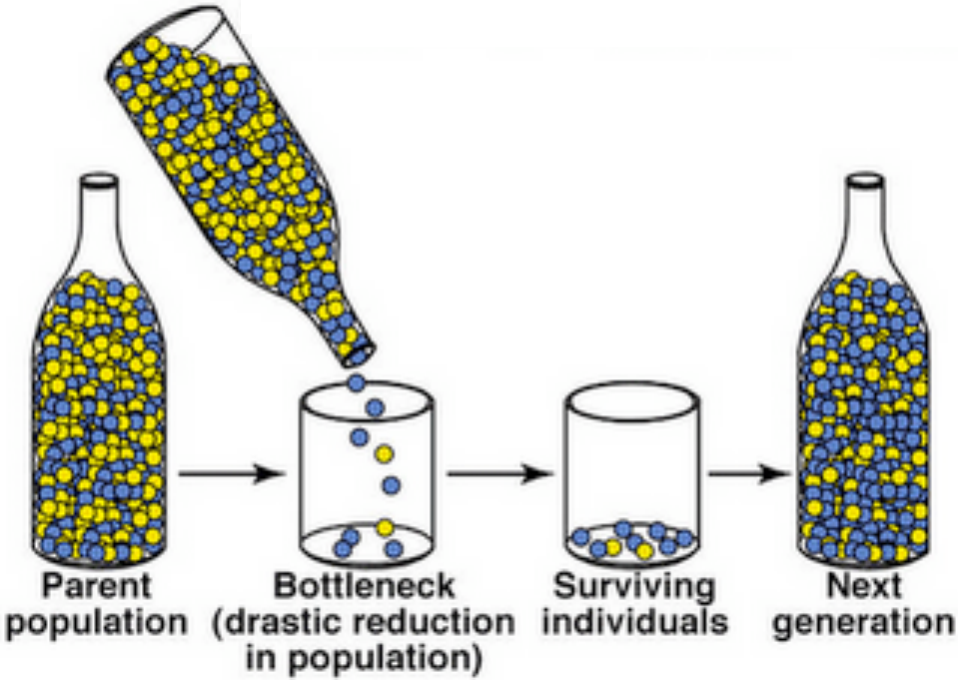
- Two primary forces affect patterns of human genetic variation

  1. Demography: changes in population size, inbreeding, etc. affect genetic variation through "genetic drift"

  2. Natural selection: mutations that affect the ability to survive and reproduce

Demographic History: Population Bottlenecks

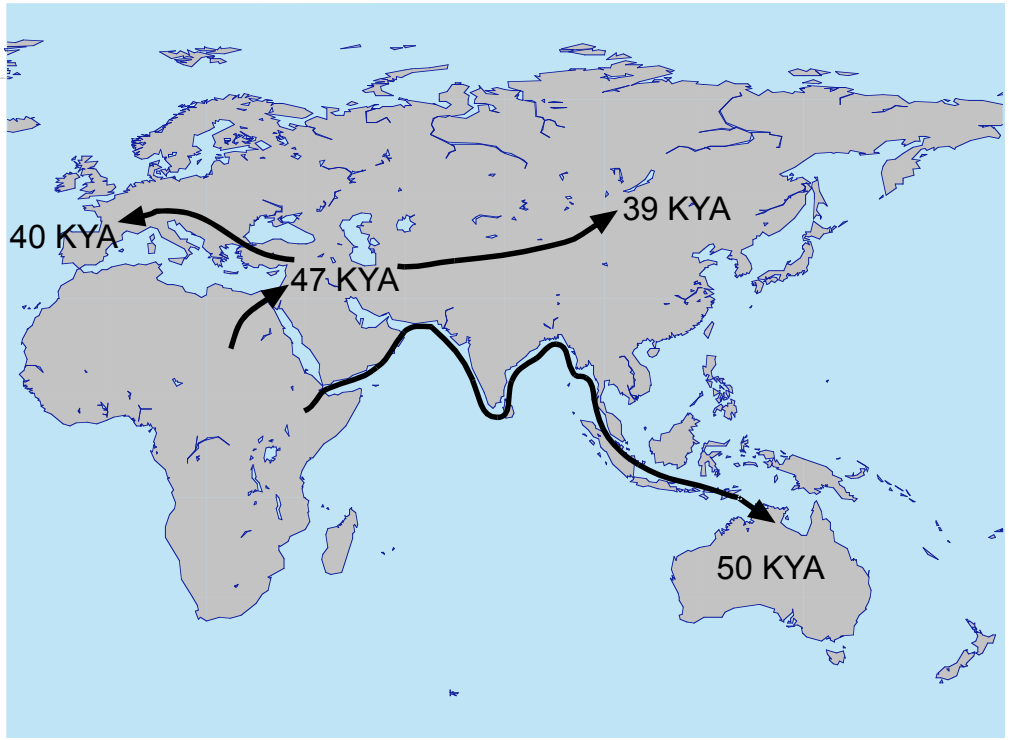
- Migration into new parts of the world often done by only a small number of individuals



- Random change in allele frequencies

Natural Selection

- Different types of natural selection
- Darwinian selection = adaptive evolution ≈ positive selection
- What selective pressures have existed in human history?



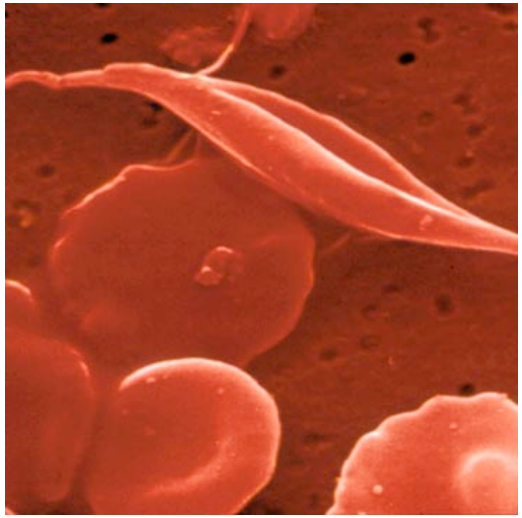
- diet
- climate
- pathogens

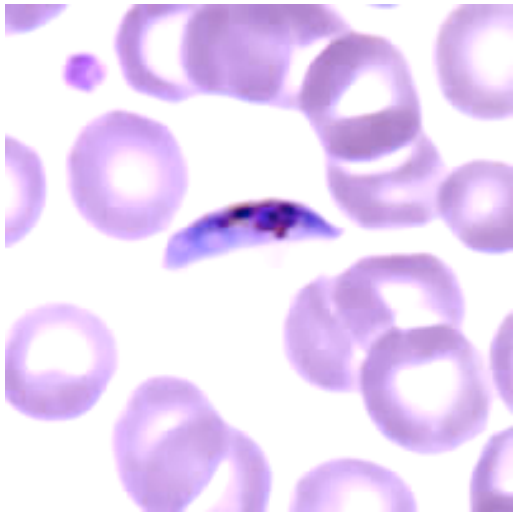
Local Adaptation: *HBB* and Sickle-cell anemia

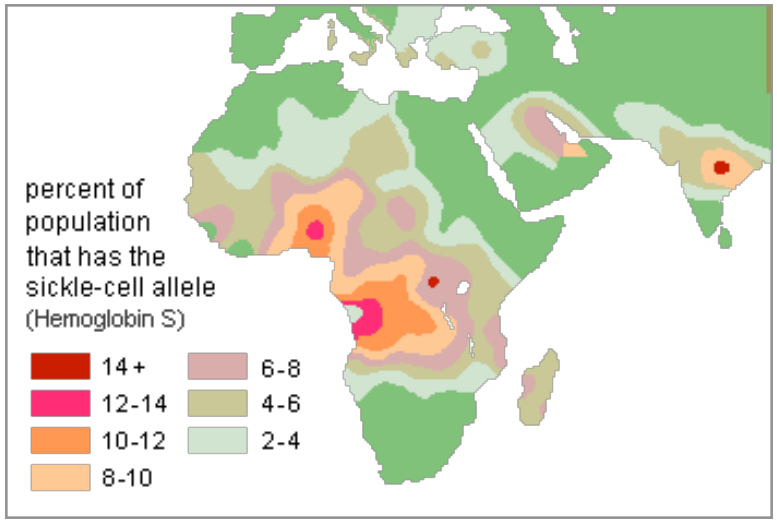
Aa heterozygotes partially protected against malaria

But aa homozygotes suffer adverse health effects

Heterozygote advantage - but only where malaria is present







Can lead to large allele frequency differences at specific loci among populations

General Evolutionary Misconceptions

Misconception 3: Humans represent the zenith of evolution

Misconception 4: Adaptive evolution in population x means that population x is more evolved than other populations

Take Home Points

- Anatomically modern humans emerged in Africa ~ 100-150 Kyr
- ~ 50 Kyr "Out of Africa" migration
- Most genetic variation is found within not between populations
- However, genetic structure does exist among human populations
  - genetic drift (population bottlenecks, inbreeding, etc.)
  - adaptive evolution
- Genomic distribution of human genetic variation reflects our past and shapes the spectrum of phenotypic variation and disease susceptibility

Where next?

Genome 411, Gene Action

Genome 465, Advanced Human Genetics

Genome 373, Genome Informatics

Genome 490, Undergraduate seminar

Genome 372, Genomics and Proteomics

Genome 453, Genetics of the Evolutionary Process

Thanks to…

Anne and her gang of TAs

All of your questions and class participation

“Before I came here I was confused about this subject. Having listened to your lectures I am still confused… but on a higher level.”

– Enrico Fermi