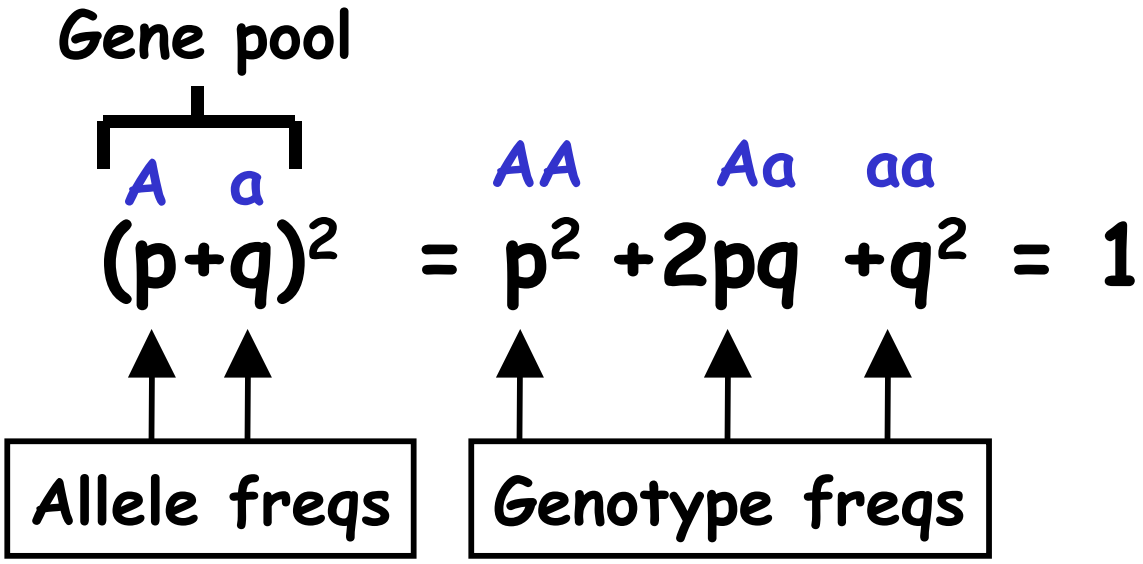
Bio 97

Population Genetics II

1. Forces that keep "bad" alleles in gene pools
2. Inbreeding

Population Genetics

Hardy Weinberg Law:



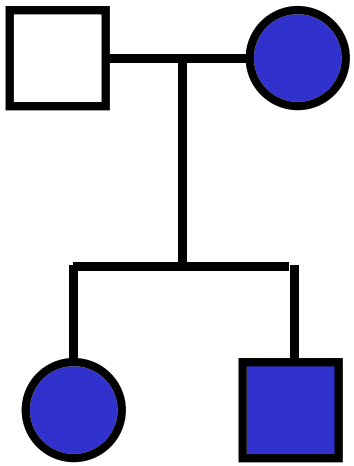
HW equilibrium: allele freqs remain constant from generation to generation, under certain conditions

Hi Professor,

The disease is called Sickle Cell Anemia and I only know that my mom, brother, and I have it. I did some research on it and it says it's an autosomal recessive disease. I tried asking my mom if she knew anyone else in her family that has it, but my mom said she wouldn't know.

I've also heard from a source that globally, it effects certain races near areas where malaria is present, like it's somewhat of a resistance to that disease. Is this true and if so, would that mean it's a gene mutation?

Thanks professor



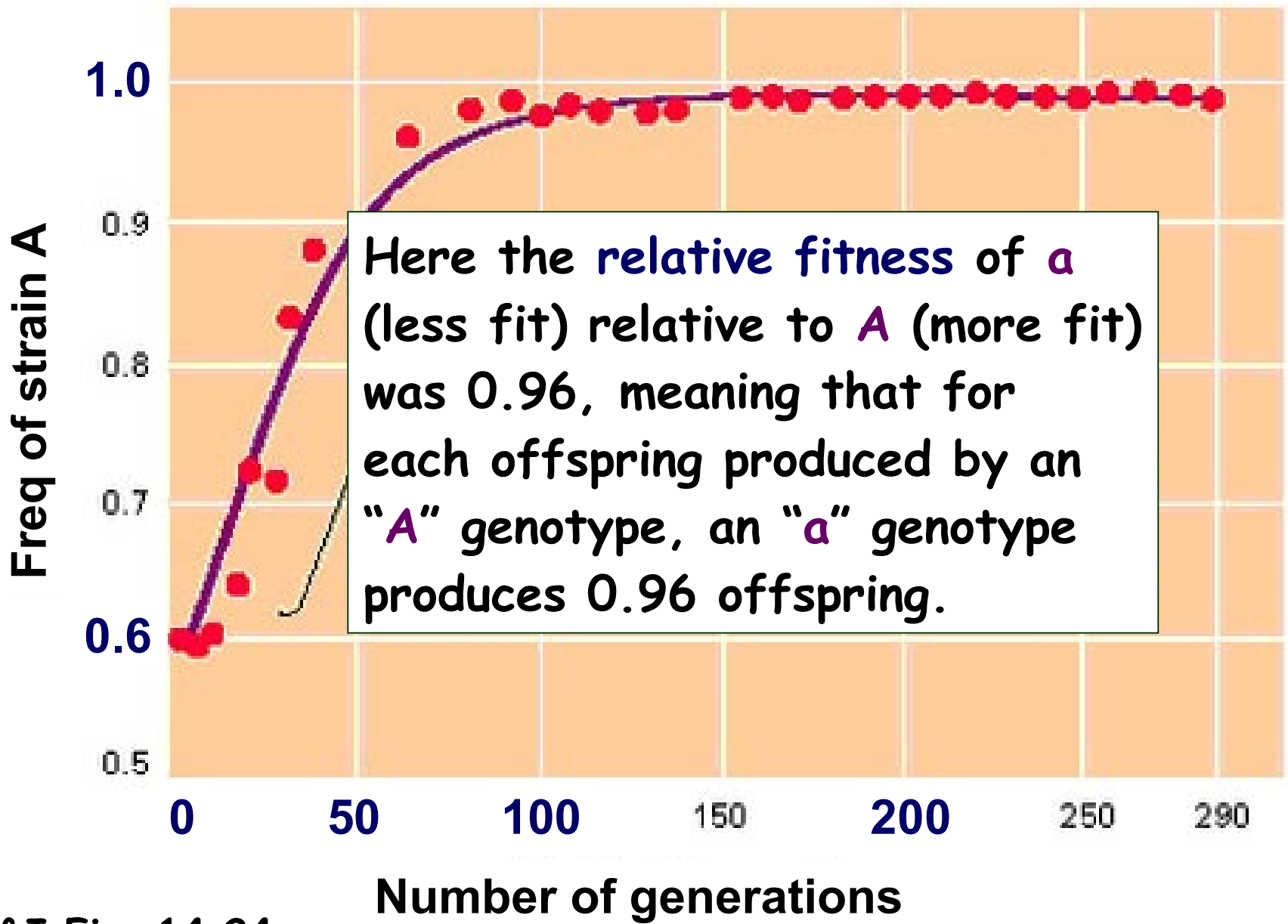
Forces that keep "bad" alleles in gene pools

- Delayed age of onset (e.g. Huntington's)
- Slow selection against recessive alleles in diploids
- Mutation-selection equilibrium
- Heterozygote superiority

Sometimes, bad alleles become good

Selection for/against dominant alleles is efficient

- A very weak selective advantage can still lead to an allele becoming fixed (= the "only" allele in the pop)
- (genetic drift finishes it off)
- True for haploids, and for dominant alleles in diploids


Freq of strain A
1.0
0.9
0.8
0.7
0.6
0.5
0
50
100
150
200
250
290
Number of generations
Here the relative fitness of a (less fit) relative to A (more fit) was 0.96, meaning that for each offspring produced by an "A" genotype, an "a" genotype produces 0.96 offspring.

H&J Fig. 14.24

On the other hand...

- Genetic drift can result in a very good, dominant allele being eliminated from the population
- The vast majority of good alleles/genes that arose during our evolution did not end up in our gene pool

Selection for/against recessive alleles is inefficient

- When the allele is rare
- Why? - because then most recessive alleles are in heterozygotes
- Thus, rare disease-causing recessive alleles persist in the population in heterozygote carriers, even if they are lethal when homozygous

Assuming HW…

$$\frac{\#\text{ alleles in carriers}}{\#\text{ alleles in affected}} = \frac{2pq}{2q^2}$$

$$= \frac{p}{q} \qquad = \frac{(1-q)}{q} \cong \frac{1}{q}$$

$q^2 = 1/10{,}000$; $q = 1/100$, …

Carrier/Affected Ratio for an autosomal recessive disease

Disease Incidence	Carrier Frequency	Ratio Carrier/Affected
0.1	0.43	4.3
0.01	0.18	18.0
0.001	0.06	61.2
0.0001	0.02	198.0

q2 2pq

Selection vs. Mutation

- New mutations often generate harmful alleles
- Selection can be balanced by new mutations
- At equilibrium, new alleles are created by mutation at the same rate they are removed by selection

eq: q^2 = mutation rate

(for strictly recessive, lethal/sterile allele)

We're all genetically defective

For any essential gene in our genome that's

At mutation-selection equilbrium…

q^2 = mutation rate = 10^{-5} = 1/100,000

$q \cong 3/1000$, $2pq \cong 6/1000$

- The chance that you are a carrier of a defective, recessive allele for a given essential gene is 0.6%
- As we may have >2,000 essential genes, you may well be a carrier for over 12 different lethal "diseases"

Heterozygote Superiority

- Fitness (a measurement of viability and fertility) of heterozygote is greater than either homozygote
- Example: sickle cell anemia - heterozygote carriers are more resistant to malaria
- HS keeps both alleles in gene pool
- Example of a "bad" allele becoming good

Malaria

- A serious, sometimes fatal, infectious disease
- 300-500 million cases annually;
- Over 1 million deaths "
- Flu-like symptoms, anemia, jaundice, possibly -> kidney failure, coma, death
- Risk areas - large parts of:
  - Central/South America
  - Africa
  - Indian subcontinent
  - Southeast Asia
  - Middle East
  - Oceania

Malaria

- Caused by infection with the parasite *Plasmodium*

- Transmitted by mosquito bites

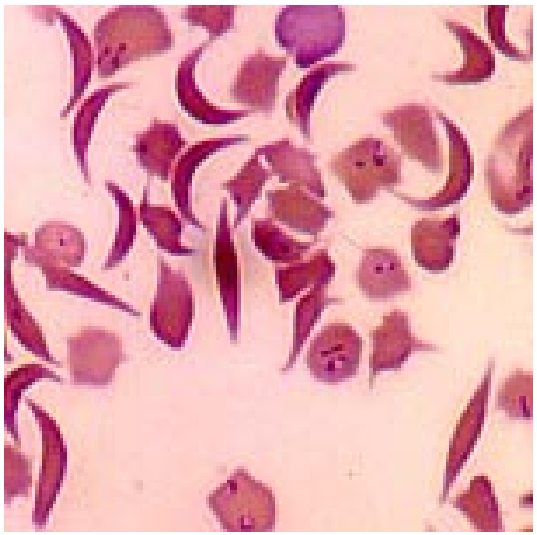
- Pm Lives in liver cells and red blood cells
- Kills RBCs and releases toxins into bloodstream
- Symptoms may not show up for 1 yr after bite (travelers be vigilant)

- Studied by Dr. Tony James

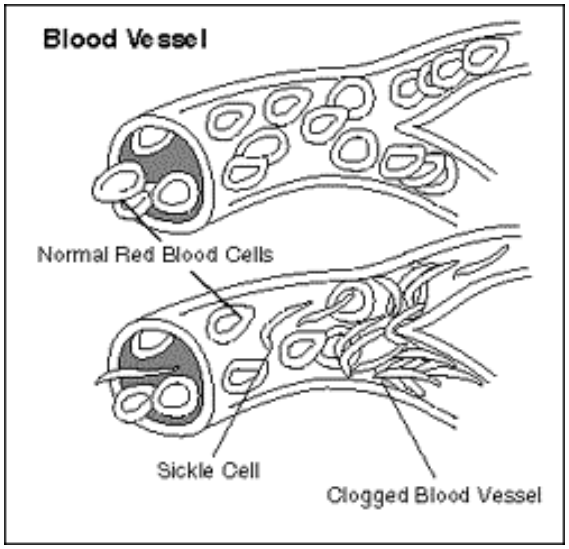
Sickle-Cell Anemia

Disease of the Day

- Autosomal recessive
- Gain-of-function mutation (E6V) in the gene encoding the β chain of hemoglobin (found in RBCs, carries oxygen)
- Sporadic vessel clotting causes acute pain, organ failure
- Incidence 1/500 among african americans



- Carriers cells don't normally sickle
- If infected by Pm, they do
- This kills the Pm



INBREEDING

Problem

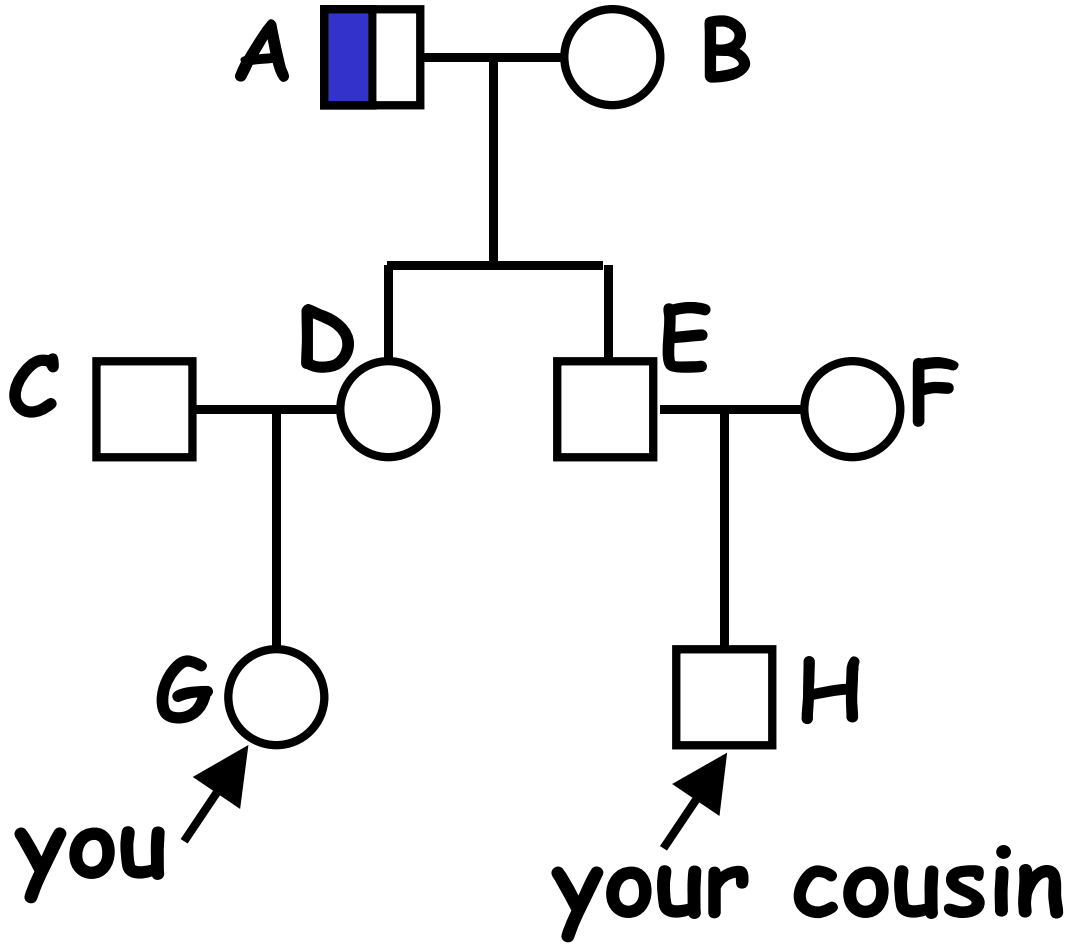
Assume your grandfather is a carrier (heterozygote) of a very rare genetic disease (autosomal recessive, incidence 1/250,000).

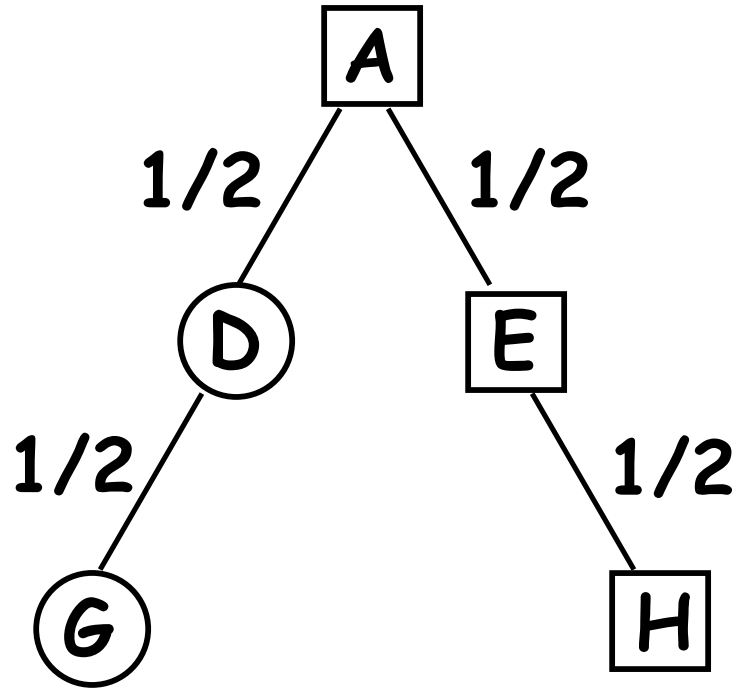
(A) What's the chance that both you and your first cousin are carriers of this disease?

A. 1/4 B. 1/16 C. 1/1000 D. 1/62,500

HINT

- $q^2 = 1/250{,}000$
- $q = 1/500$
- $2pq \cong 1/250$
- You don't need to know this to solve the problem





1/2 x 1/2 x 1/2 x 1/2 = 1/16

= fraction of alleles that G & H share from common grandfather

A. 1/4 = fxn of grandpa's allele that you have = Chance that you are a carrier

B. 1/16 = correct answer = fxn of grandpa's allele that you and your cousin share = 1/4 x 1/4

C. 1/1000 = chance that you and an unrelated person are both carriers = 1/4 x 1/250

D. 1/62,500 = chance that any two people in the general population are both carriers = $(1/250)^2$

First cousin mating would increase the risk over 60-fold

Inbreeding

- **Individual:** Increases the risk of having a kid homozygous for a rare recessive allele
- **Population:** Results in an excess of homozygotes compared with random mating

Do any of these populations show signs of inbreeding?

- Are they in HW equilibrium ?

	AA	Aa	aa
Pop#1	.25	.50	.25
Pop#2	.36	.28	.36
Pop#3	.36	.48	.16

Use allele counting

(p = AA + 1/2 Aa)

	AA	Aa	aa	p	q	2pq	
Pop#1	.25	.50	.25	.5	.5	.5	✓
Pop#2	.36	.28	.36	.5	.5	.5	
Pop#3	.36	.48	.16	.6	.4	.48	✓

Inbreeding --> heterozygote freq. < 2pq

Is modern medical science ruining our gene pool?

Does saving the life of people with recessive genetic diseases decrease the fitness of our population?

(in class discussion)

People with untreatable genetic diseases should be "encouraged" not to have children

What do you think about this statement?

People with bad genes should be forcibly sterilized

Please provide me with arguments against this statement