

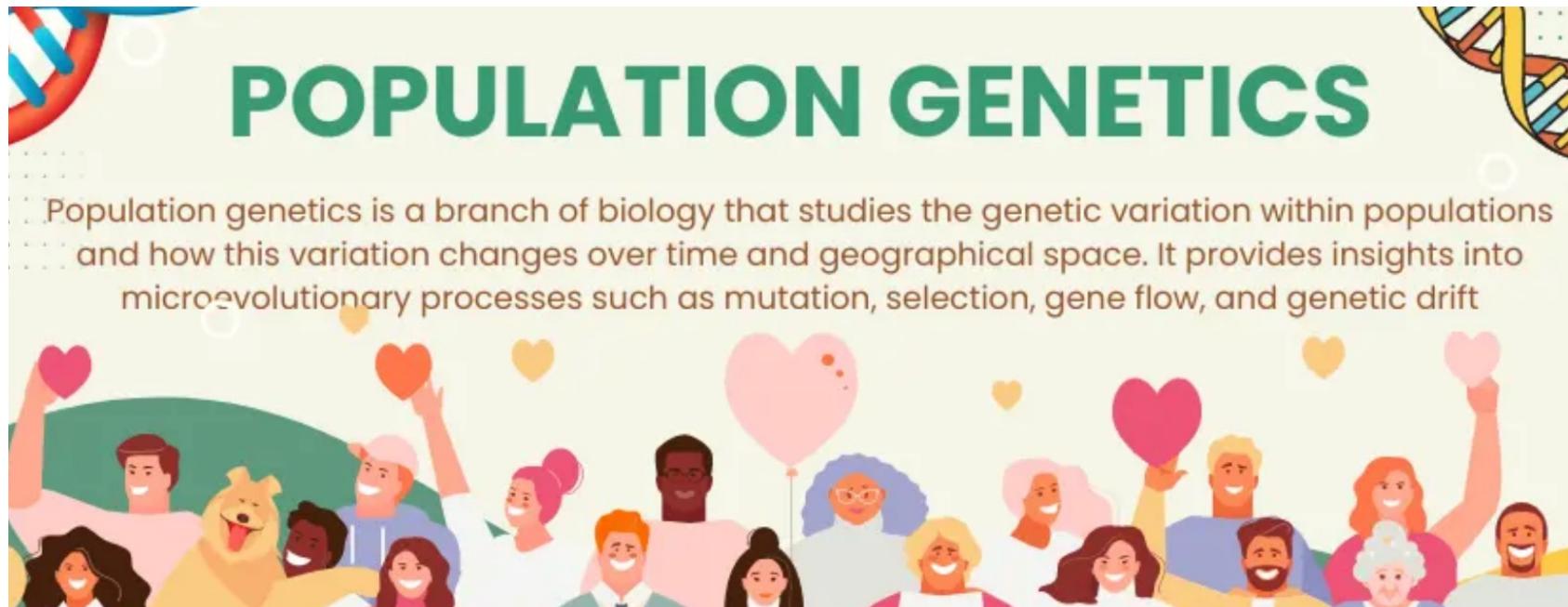
# *Population and Quantitative Genetics (5 lectures)* Prof. Schoen

## **Module: Population Genetics (first 2.5 lectures)**

Lecture 10 — Genes in populations. **Hardy-Weinberg theory.**

Lecture 11 — Inbreeding. Mutation and migration. Genetic drift.

Lecture 12 — The genetics of natural selection. Intro to Quantitative genetics.



*When there is random mating, no mutation, no selection, no migration and no drift, the genotype frequencies in the next generation are frequencies in the cells of this table:*

		Eggs:	
		$A (p)$	$a (q)$
		$AA$	$Aa$
Sperm: $A(p)$	$A(p)$	$p^2$	$pq$
	$a(q)$	$pq$	$q^2$
		$Aa$	$aa$

*These are referred to as:  
“Hardy-Weinberg proportions”  
or  
“Hardy-Weinberg genotype fqs”*

$$\text{Freq}(AA) = p^2$$

$$\text{Freq}(Aa) = 2pq$$

$$\text{Freq}(aa) = q^2$$



*Cystic Fibrosis (CF), a recessive disease, occurs in 4 out of 10,000 persons. Assume that the genotypes at the locus underlying CF are present in Hardy-Weinberg proportions in the human population. What is the frequency of carriers (heterozygotes) in the population?*



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- A. 0.0004
- B. 0.0008
- C. 0.0392
- D. 0.0004
- E. None of the above

*Cystic Fibrosis (CF) occurs in 4 out of 10,000 persons. Assume that the genotypes at the locus underlying CF are present in Hardy-Weinberg proportions in the human population.*

*What is the frequency of carriers (heterozygotes) in the population?*

Genotype	Phenotype	Frequencies:	
		Expected	Observed
AA	Normal	$p^2$	?
Aa	Normal (Carrier)	$2pq$	?
aa	CF	$q^2$	0.0004

*If the freq(aa) = 0.0004, the frequency of the a allele must therefore be  $q = (0.0004)^{0.5}$*

*That is,  $q = 0.02$*

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If the  $\text{freq}(aa) = 0.0004$ ,  
the frequency of the  $a$  allele must therefore  
be  $q = (0.0004)^{0.5}$

That is,  $q = 0.02$

$$\begin{aligned} * \text{So, } 2pq &= 2(0.98)(0.02) \\ &= 0.0392 \end{aligned}$$

**Ratio of carriers:diseased**  
 $= 2pq/q^2 = 0.0392/0.0004$   
 $= 98$

# DNA fingerprinting



## Arrest made in 1994 cold case murder of Virginia mother after DNA testing, confession: Police

Robin Lawrence, 37, was found dead in her Springfield home in 1994.

By [Beatrice Peterson](#)

September 12, 2023, 12:21 AM



## The Gazette



Quebec / News / Local News

## Police tracked Quebec cold case suspect to cinema, seized drinking cup, trial hears

*The Crown has said the genetic material on the cup and straws was matched to DNA found at the crime scene 22 years earlier.*

PEI

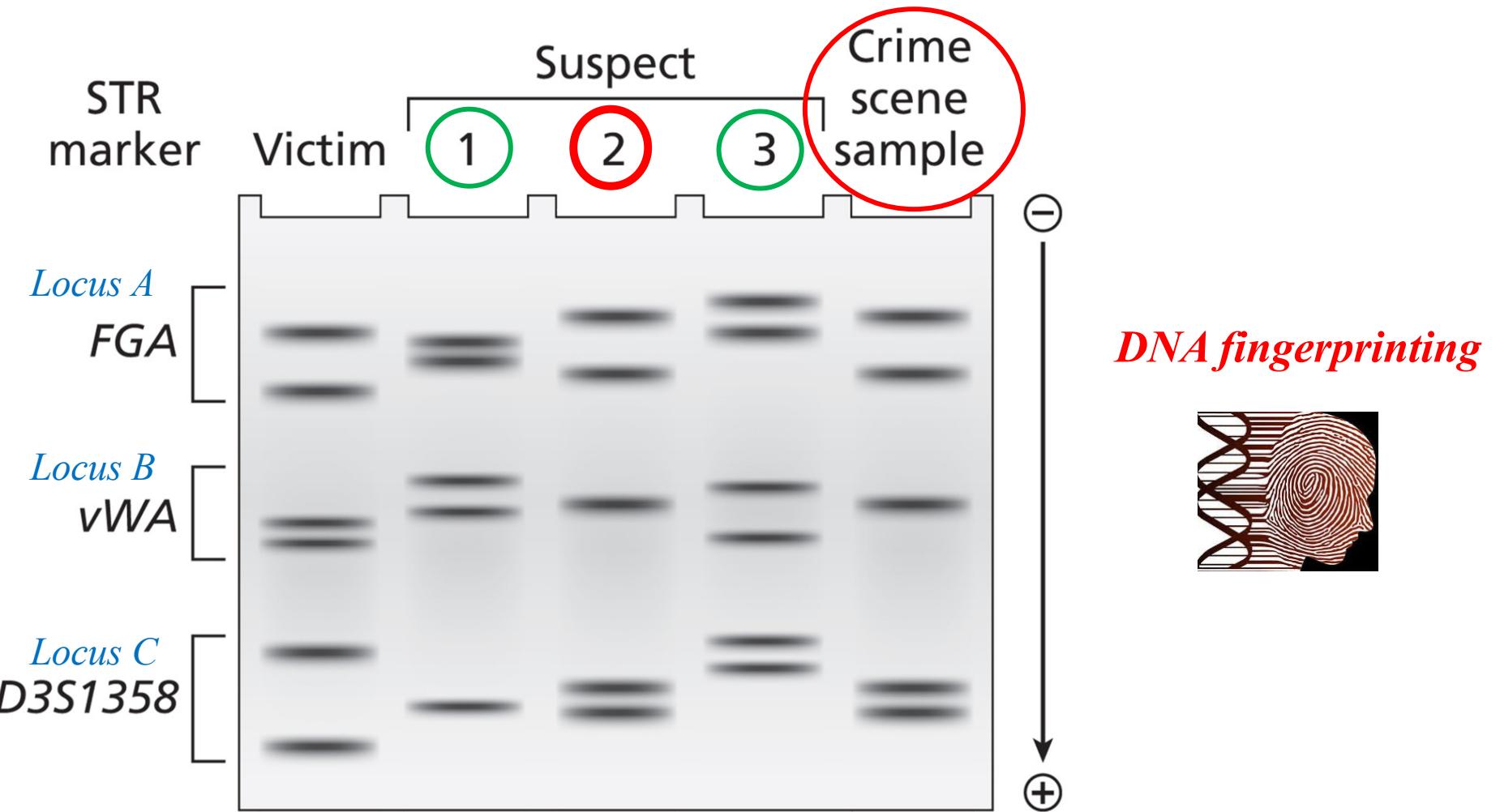
## After 35 years, DNA evidence leads to 1st-degree murder charge in P.E.I. cold case

Todd Joseph Gallant, 56, arrested in death of 'respected teacher' Byron Carr



[Stephen Brun](#) · CBC News · Posted: Jan 26, 2024 6:53 AM EST | Last Updated: January 26







*A suspect in a crime has the following genotype at three separate and unlinked biallelic loci, A, B and C: A1/A2; B2/B2; C2/C2. Blood found at the scene of the crime is seen to match this genotype. The allele frequencies of alleles A1, B1, C1 in the population are 0.9, 0.8, and 0.7, respectively.*

*What is the probability that this match occurs in the general population? (Assume Hardy-Weinberg proportions for each locus)*

A suspect in a crime has the following genotype at three separate and unlinked biallelic loci, A, B and C:  $A1/A2$ ;  $B2/B2$ ;  $C2/C2$ . Blood found at the scene of the crime is seen to match this genotype. The allele frequencies of alleles A1, B1, C2 in the population are 0.9, 0.8, and 0.7, respectively.

What is the probability that this match occurs simply by chance alone?  
(Assume Hardy-Weinberg proportions for each locus)

- A. 0.432001
- B. 0.055440
- C. 0.000648
- D. 0.000493

A suspect in a crime has the following genotype at three separate and unlinked biallelic loci, A, B and C:  $A1/A2$ ;  $B2/B2$ ;  $C2/C2$ . Blood found at the scene of the crime is seen to match this genotype. The allele frequencies of alleles A1, B1, C1 in the population are 0.9, 0.8, and 0.7 respectively.

What is the chance that this match occurs in the general population? (Assume Hardy-Weinberg proportions for each locus)

$$\text{Freq } (A1/A2) = 2pq = 2(0.9)(0.1) = 0.18$$

**In-class Problem 2.** A suspect in a crime has the following genotype at three separate and unlinked biallelic loci, A, B and C:  $A_1/A_2$ ;  $B_2/B_2$ ;  $C_2/C_2$ . Blood found at the scene of the crime is seen to match this genotype. The allele frequencies of alleles A1, B1, C2 in the population are 0.9, 0.8, and 0.7 respectively.

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$$\text{Freq } (C_2/C_2) = q^2 = (0.3)^2 = 0.09$$

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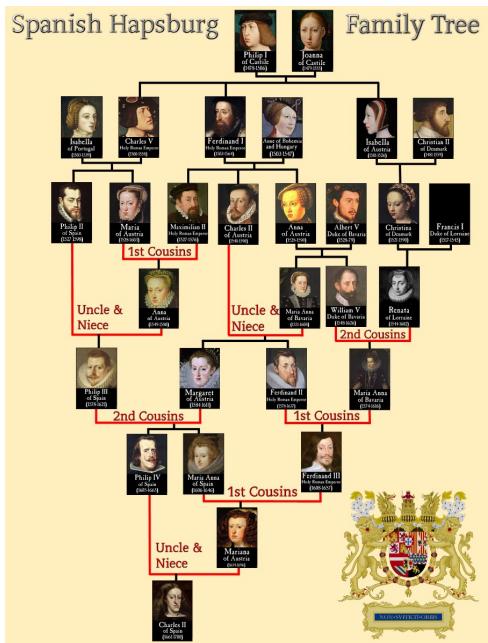
$$\text{Freq } (B_2/B_2) = q^2 = (0.2)^2 = 0.04$$

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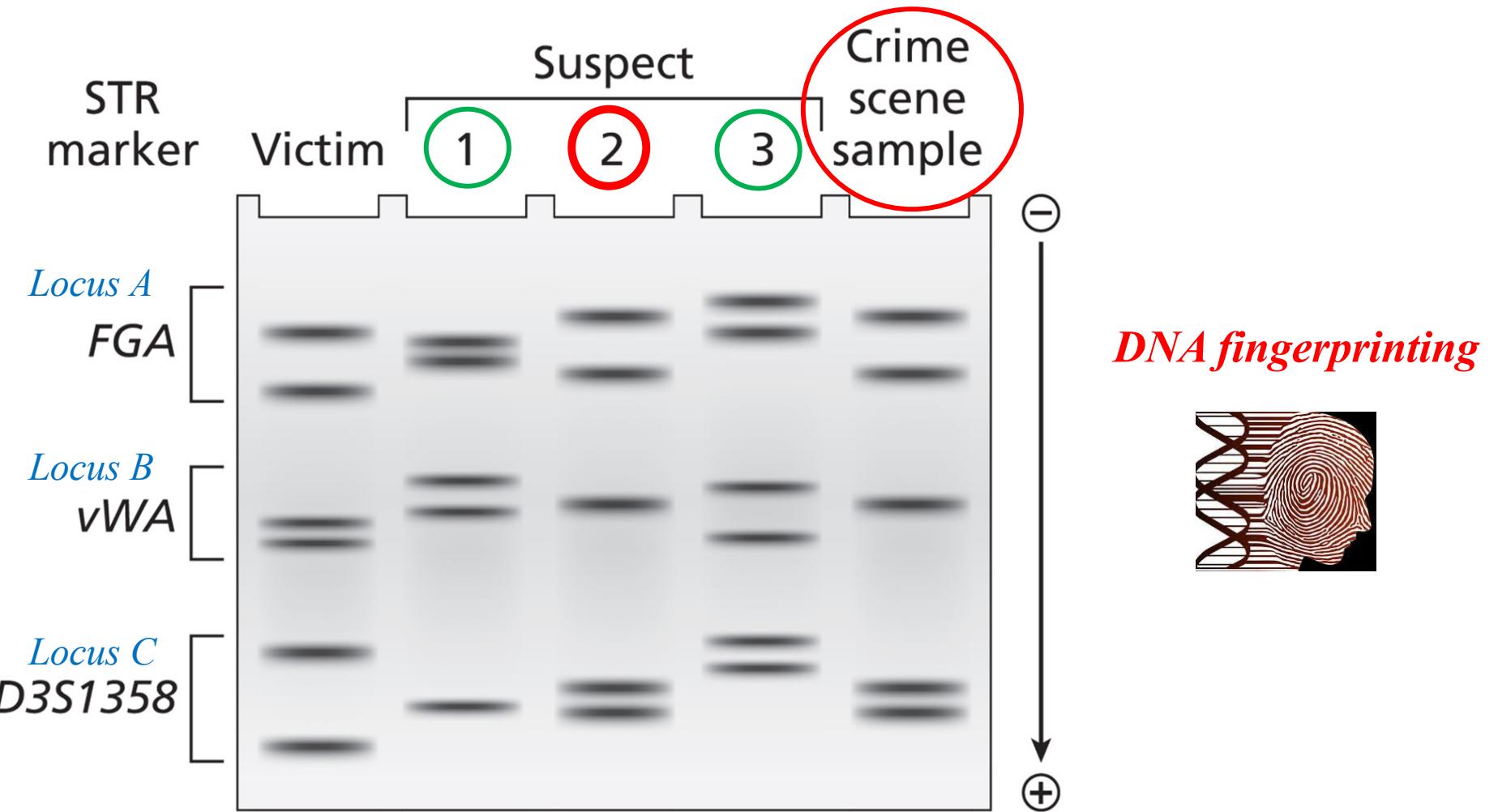
$$\text{Prob } (A_1/A_2; B_2/B_2; C_2/C_2) = 0.18 \times 0.04 \times 0.09 = 0.000648$$

## Module: Population Genetics continued

### Lecture 11—Inbreeding. Mutation, Migration, Drift



<https://www.youtube.com/watch?v=dtfRxYlO6G0>



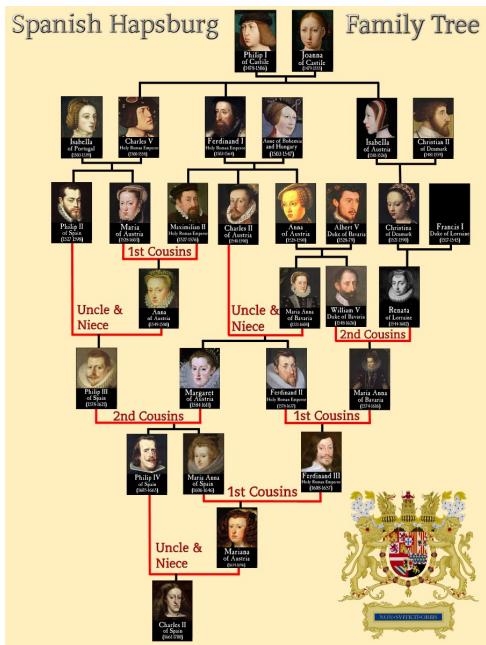
## ***Module: Population Genetics continued***

### *Lecture 11—Inbreeding. Mutation, Migration, Drift)*



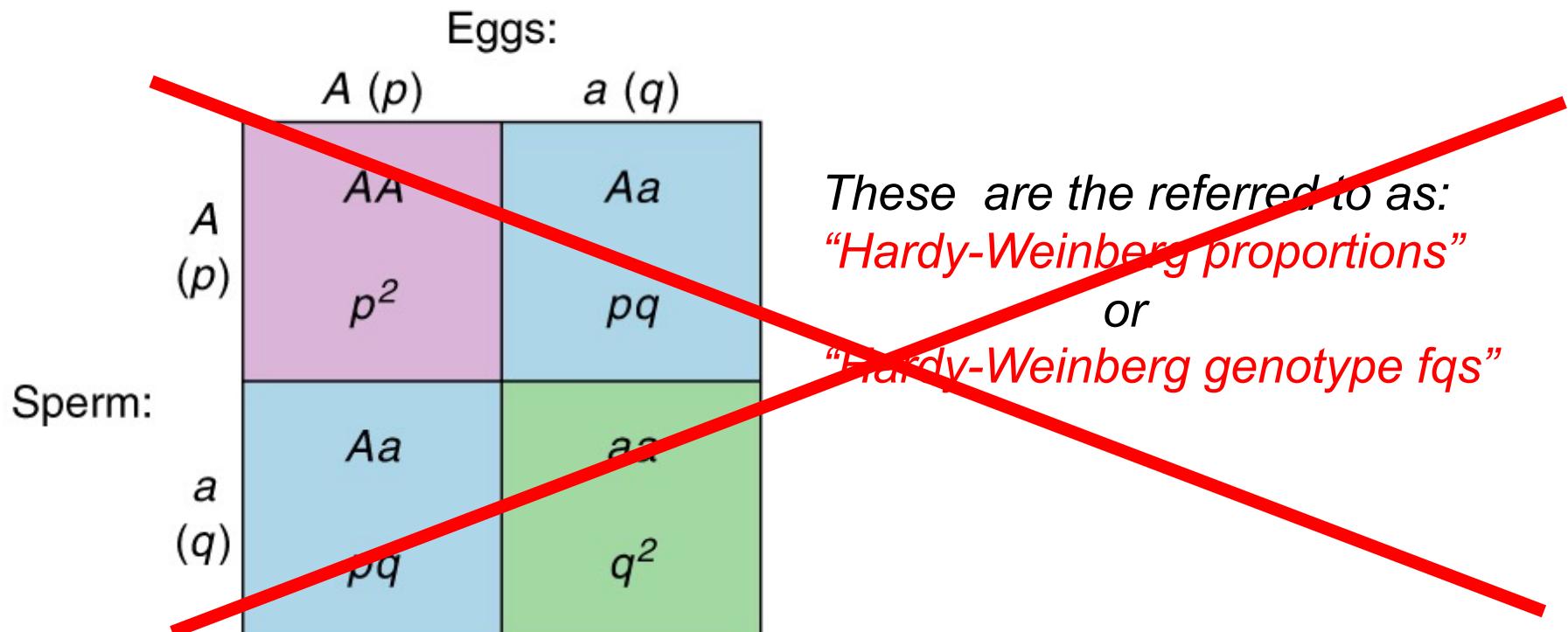
- |   |
|---|
| 1. Inbreeding (Ch18 – section 3)  |
| 2. Mutation and migration (Ch18 – section 5) (skip subsections "Recombination" & "Linkage Disequilibrium" & Box 18.5) |
| 3. Genetic drift (Ch18 –section 5 )   |

# Inbreeding (a form of non-random mating)



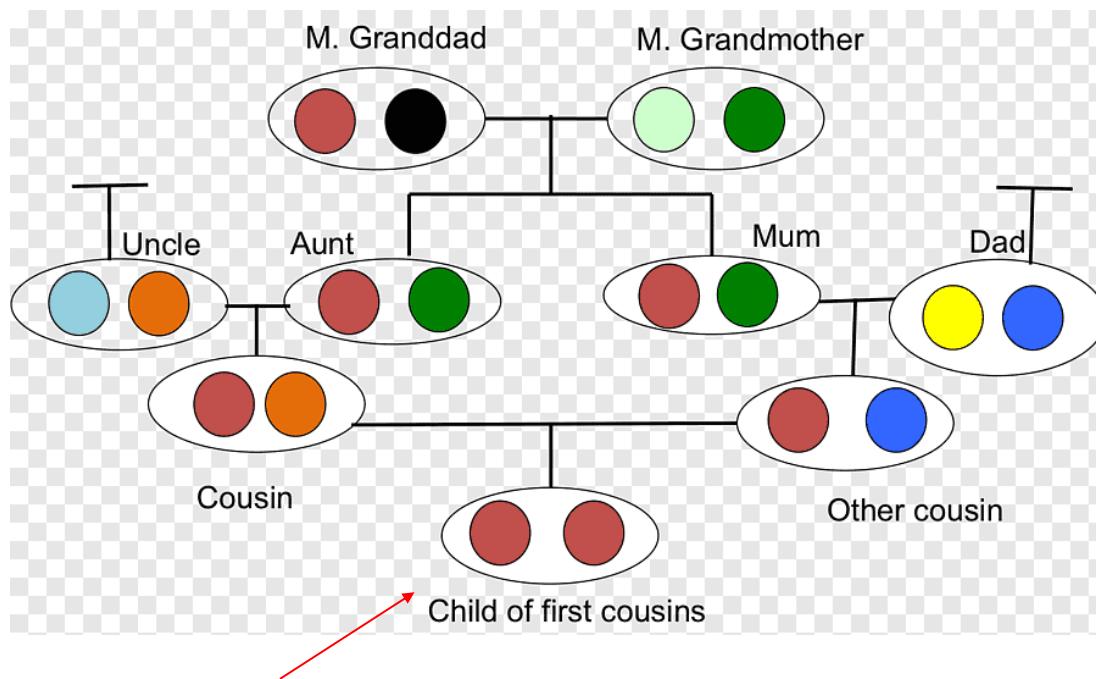
<https://www.youtube.com/watch?v=dtfRxYlO6G0>

*When there is **non-random mating**.....*



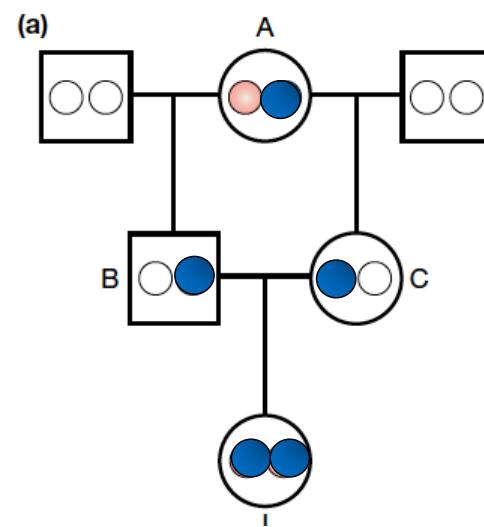
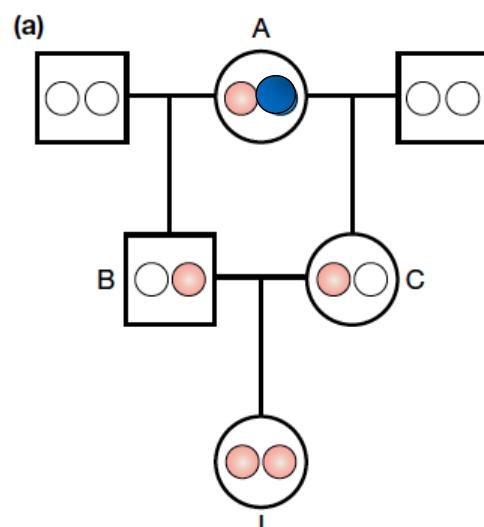
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## Inbreeding (e.g., first cousin mating)



*Alleles that are “**identical by descent**” (IBD) are one possible outcome*

## Inbreeding, identity by descent, and increased homozygosity (e.g., half brother-half sister mating, also called half-sib mating)



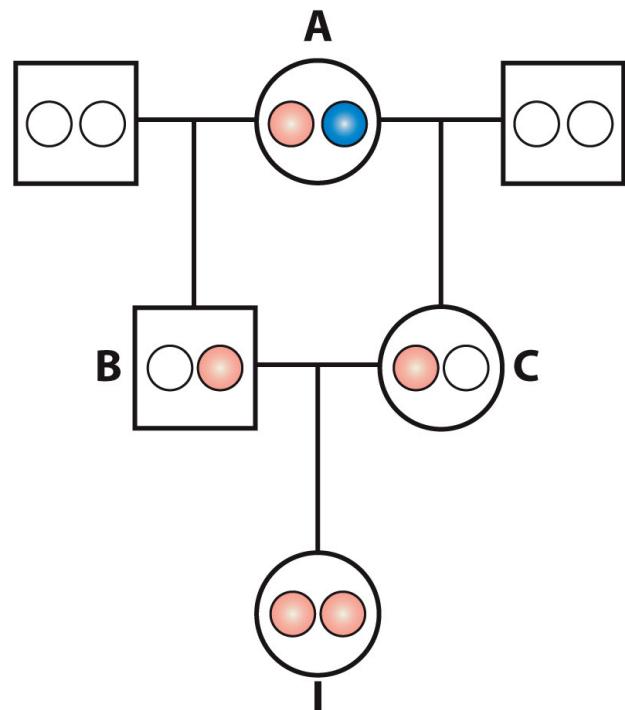
*Inbreeding increases the probability that two alleles at a locus will be copies of an allele present in an ancestor.*

**Such copies are said to be “identical by descent” (IBD)**

# The inbreeding coefficient ( $F$ )

- $F$  = the overall probability that the two alleles inherited by a given individual will be identical by descent.

## Half sib mating (calculation of the inbreeding coefficient $F$ )



- $F$  quantifies the overall probability that the two alleles inherited by a given individual will be identical by descent.
- What is  $F$  for individual I?

Figure 18-12a  
Introduction to Genetic Analysis, Eleventh Edition  
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# Pedigrees: Calculation of the inbreeding coefficient ( $F$ )

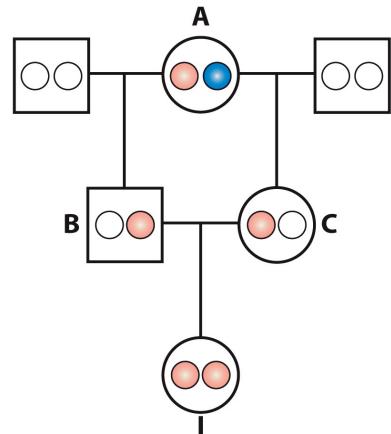


Figure 18-12a  
Introduction to Genetic Analysis, Eleventh Edition  
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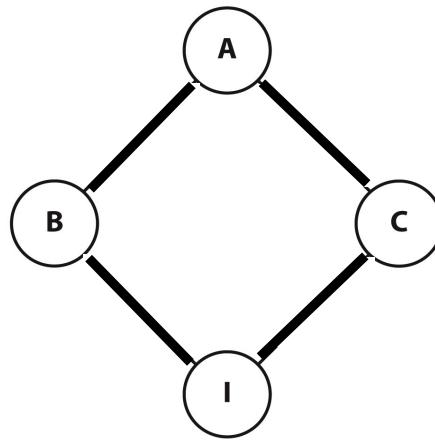
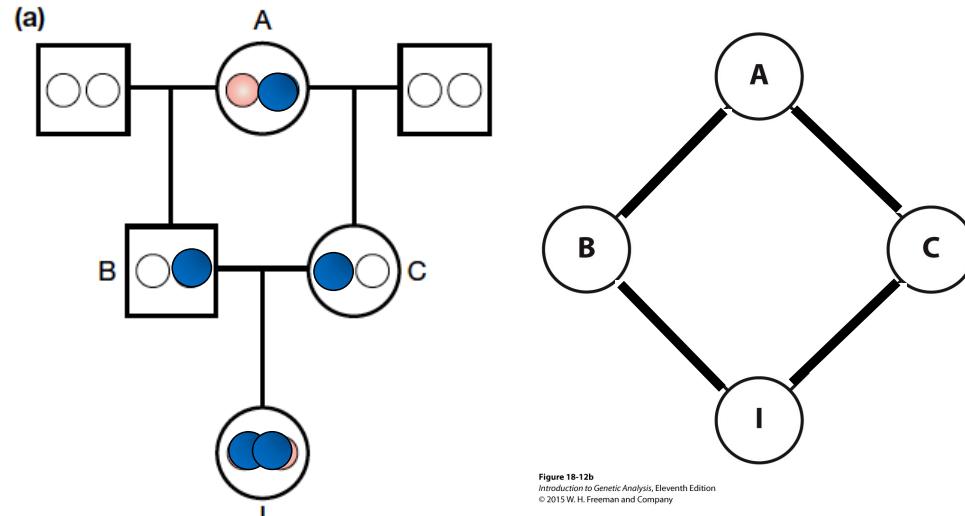
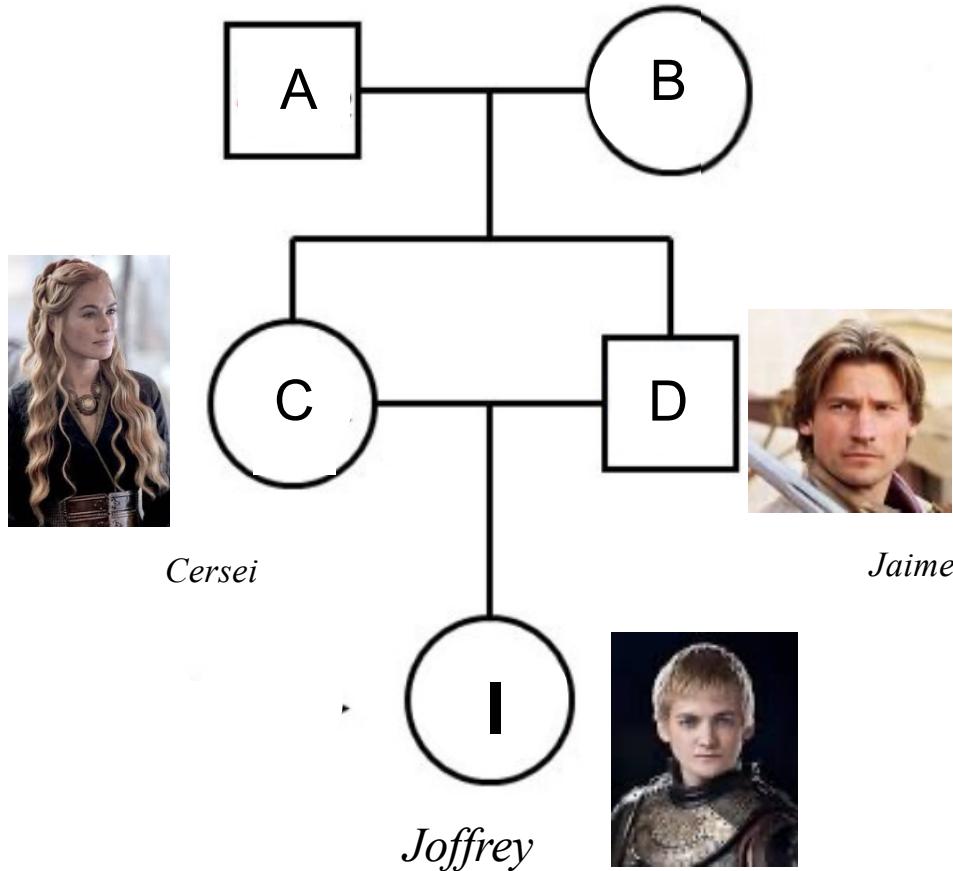


Figure 18-12b  
Introduction to Genetic Analysis, Eleventh Edition  
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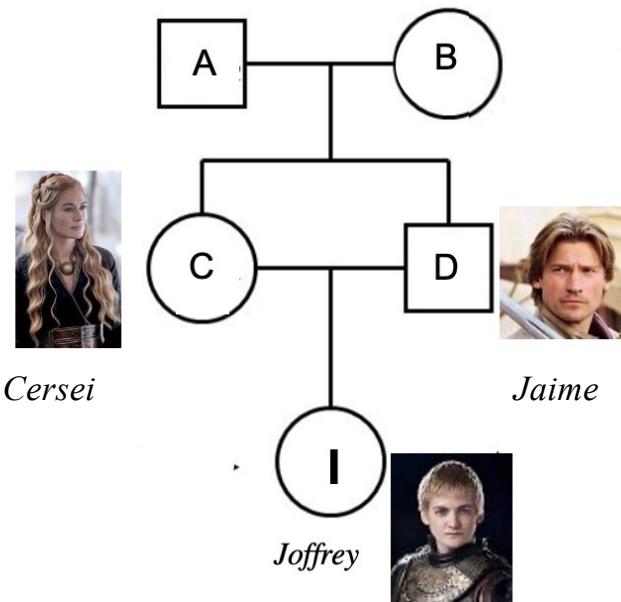
# Pedigrees: Calculation of the inbreeding coefficient ( $F$ )



**What if there is more than one common ancestor? As in Brother-sister mating (full sib mating).**



# What is Jeoffrey's Inbreeding Coefficient (F)?

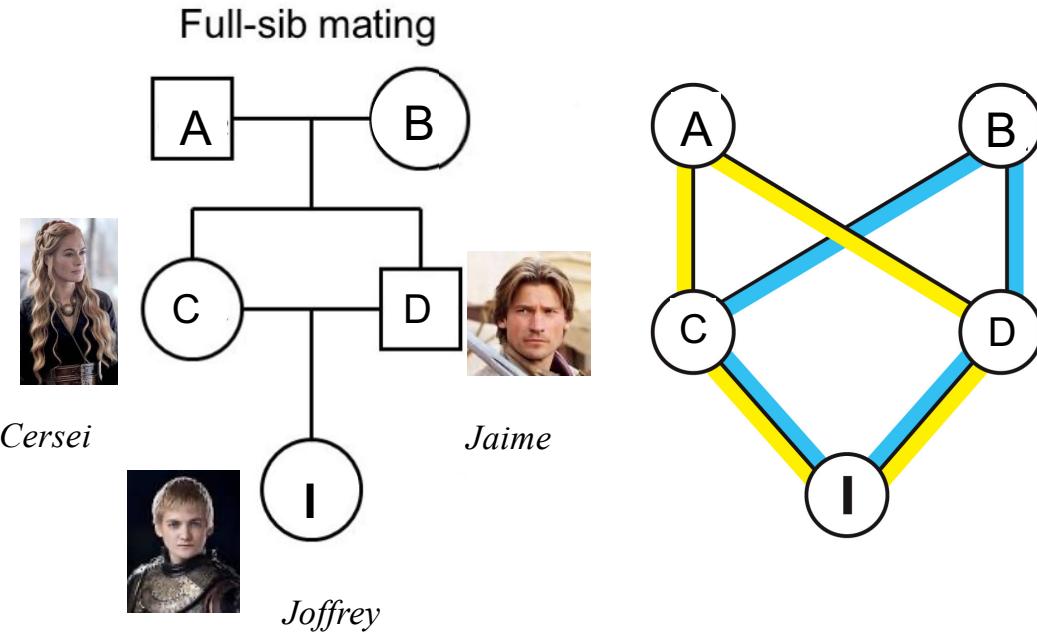




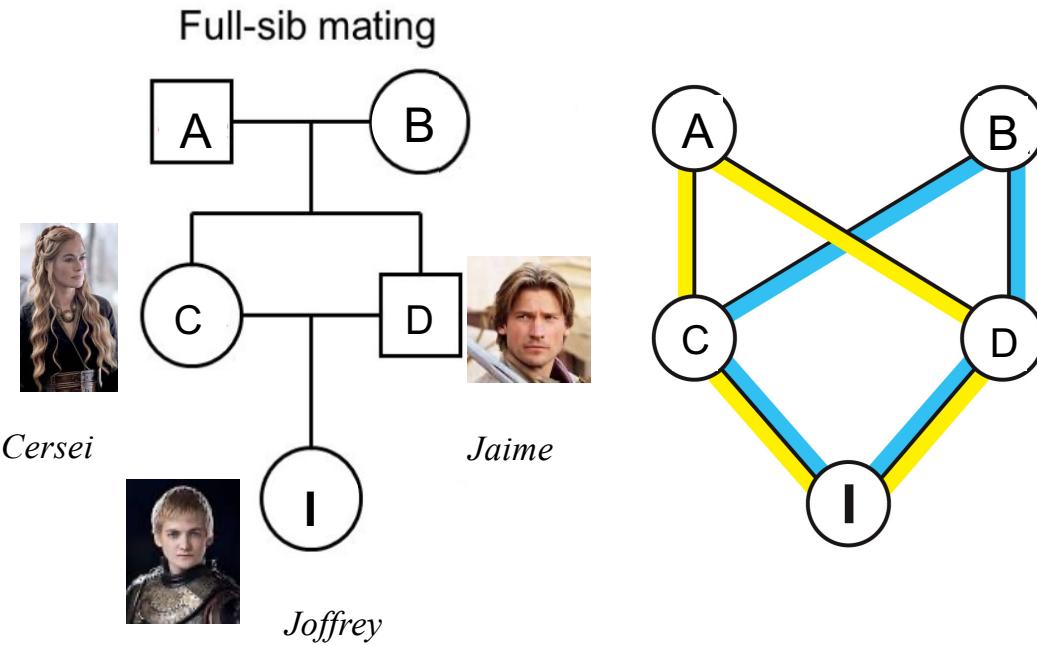
*What is Jeoffrey's inbreeding coefficient ( $F$ )?*

- A. 1/16
- B. 1/8
- C.  $\frac{1}{4}$
- D.  $\frac{1}{2}$
- E. 1

What if there is > one common ancestor? (e.g., full sib mating)



What if there is > one common ancestor? (e.g., full sib mating)



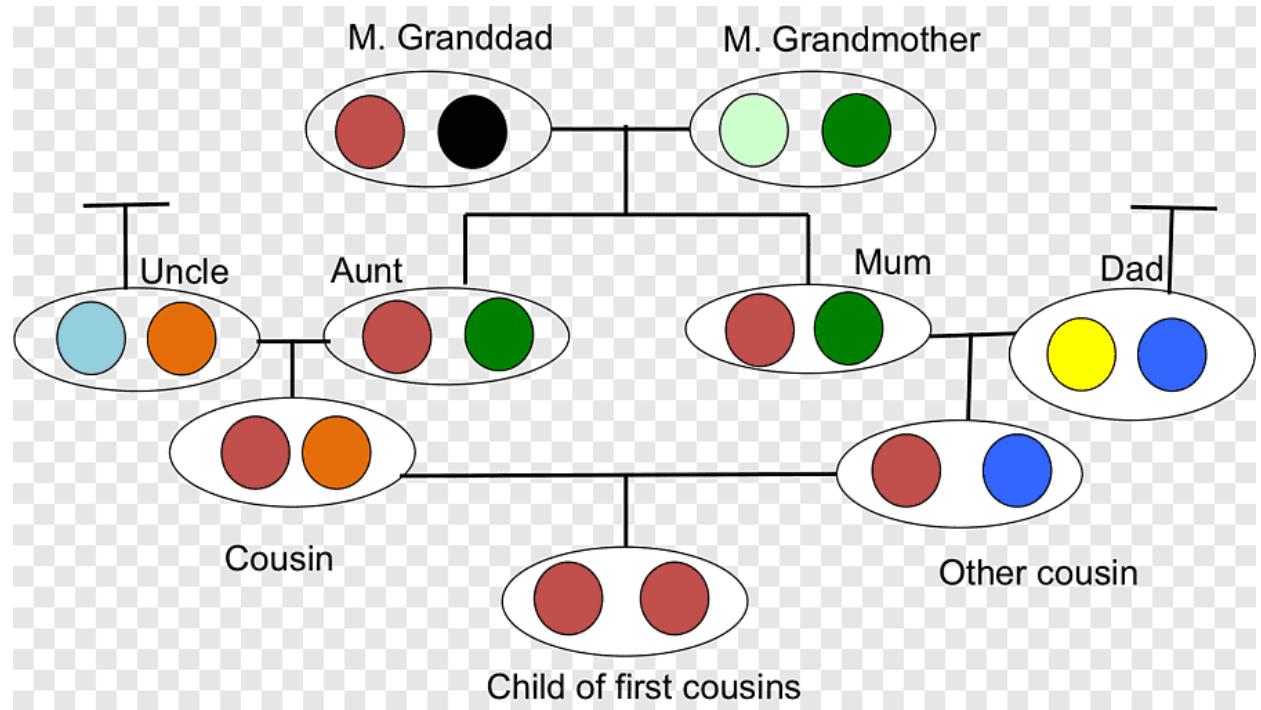


*What is Jeoffrey's inbreeding coefficient ( $F$ )?*

- A.  $1/16$
- B.  $1/8$
- C.  $1/4$
- D.  $1/2$
- E. 1



*F* is the probability that the individual inherits alleles that are identical by descent

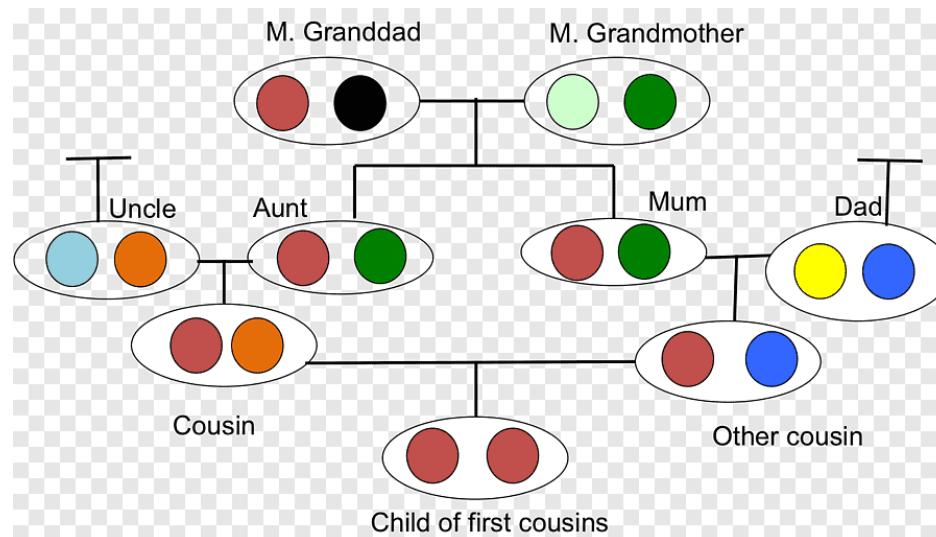


Calculate *F* for the child of a first-cousin marriage

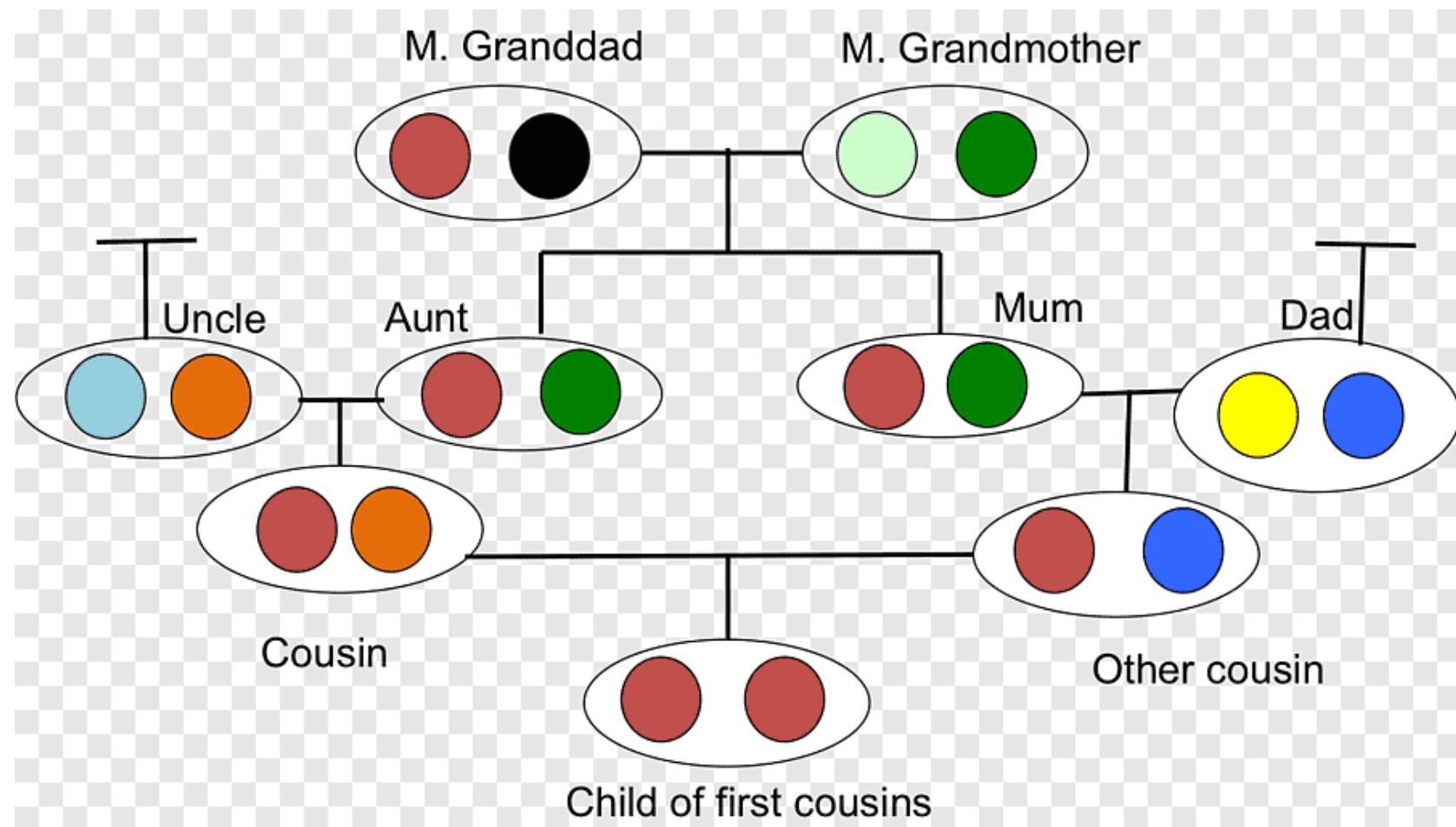


*What is F for the child of 1st cousins?*

- A.  $1/16$
- B.  $1/8$
- C.  $\frac{1}{4}$
- D.  $\frac{1}{2}$
- E. 1



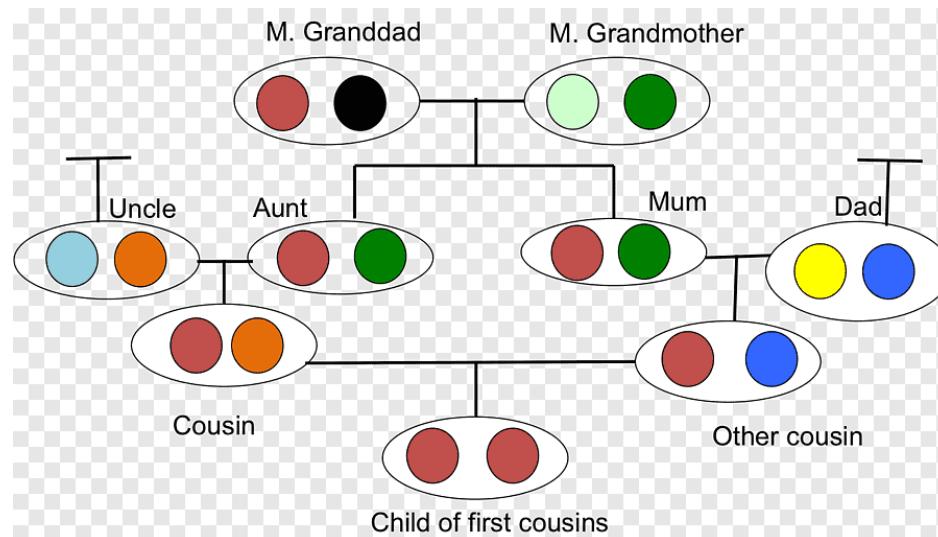
*(i) Start presenting to display the poll results on this slide.*





*What is F for the child of 1st cousins?*

- A. 1/16
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*i* Start presenting to display the poll results on this slide.

What if you had an **entire population** in which after one generation, everyone switched from random mating to mating with their 1<sup>st</sup> cousins (progeny have  $F = 0.0625$ )?

*How would the genotype frequencies in the population in the next generation differ from those expected under random mating?*

*Population with random mating*

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

$p^2$  = dominant homozygous frequency (AA)

$2pq$  = heterozygous frequency (Aa)

$q^2$  = recessive homozygous frequency (aa)

*Population with some inbreeding*

?

Inbreeding changes genotype frequencies  
(fewer heterozygotes than expected under HW conditions)

*In a population that switches over to inbreeding from random mating you would observe in the following generation:*

$$f(A_1A_1) = p^2 + Fpq$$

$$f(A_1A_2) = 2pq(1 - F)$$

$$f(A_2A_2) = q^2 + Fpq$$

*That is, there would be:  
**MORE HOMOZYGOTES***

*and*

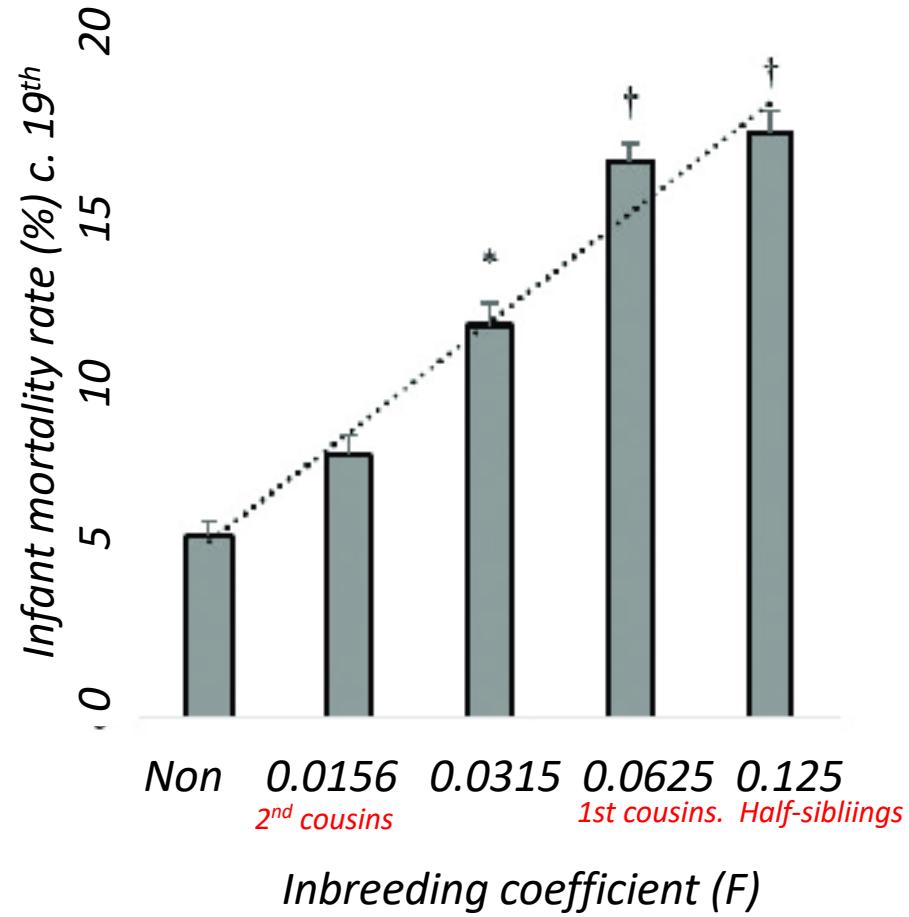
***FEWER HETEROZYGOTES**  
compared with a random mating population*

**Inbreeding depression (reduction in the viability of inbred individuals)** occurs because most **deleterious conditions are recessive** and require **two copies** of the mutation to be expressed

*For example:*

- Cystic fibro
- Sickle cell anemia
- Tay-Sachs disease
- Gaucher disease
- Alcaptonuria
- Albinisms
- etc.

## Inbreeding mortality US rate (in percent)



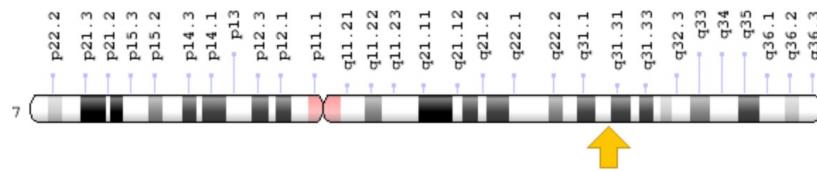
# **Evolutionary forces that change allele frequencies**

# Factors Influencing Allele Frequencies

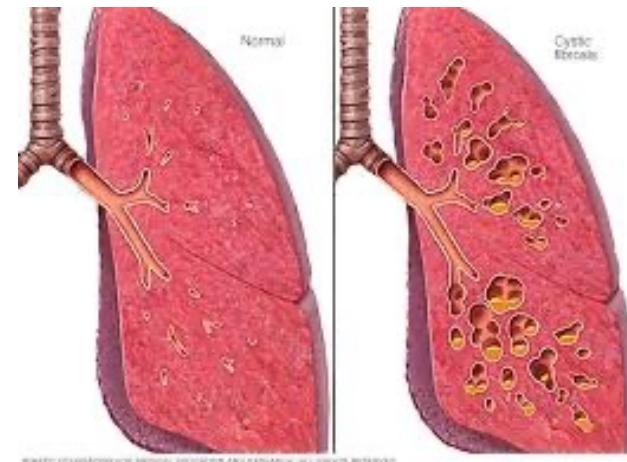
- *Mutation*
- *Migration*
- *Genetic Drift*
- *Natural Selection*

## Mutation

e.g., *Mutations at the Cystic Fibrosis Transmembrane Conductance (CFTR) locus can lead to Cystic Fibrosis*



CFTR gene is on Chromosome 7



Normal

CF lung

What do you think is a typical rate of mutation per base pair of DNA per generation in humans?

- A.  $10^{-3}$  mutations/base pair/generation
- B.  $10^{-5}$  mutations/base pair/generation
- C.  $10^{-7}$  mutations/base pair/generation
- D.  $10^{-9}$  mutations/base pair/generation

What do you think is a typical rate of mutation per base pair of DNA per generation in humans?

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### Allele Frequency Change From Mutation Alone

$A_1 \rightarrow A_2$

*mutation: rate  $u = 10^{-5}$  per generation*

*How quickly does mutation alone change allele frequencies?*

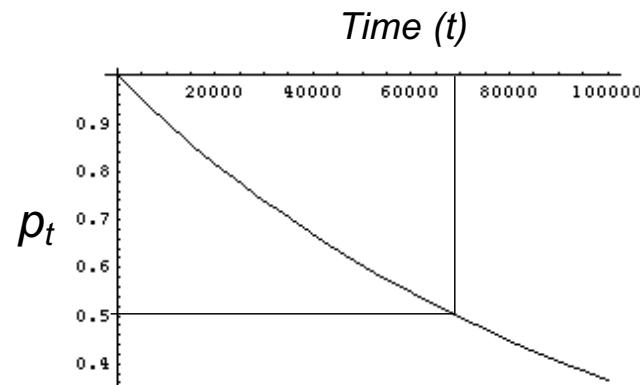
$$p_{t+1} = p_t (1 - u)$$

*Iterate the eqn.*

$$p_2 = p_1 (1 - u)$$

$$p_3 = p_2 (1 - u)$$

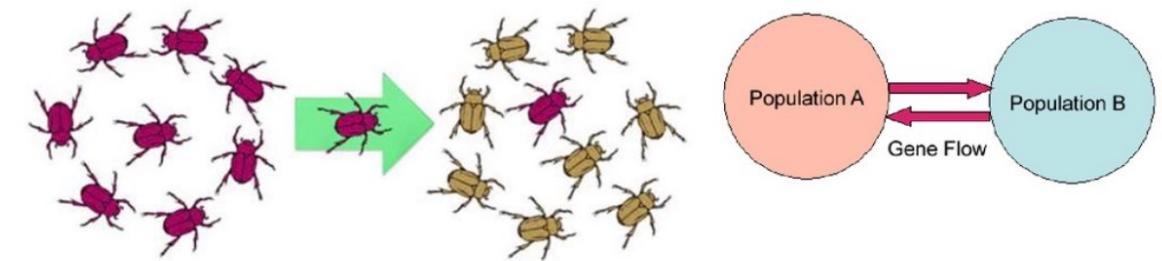
*etc.*



*Very slowly.*

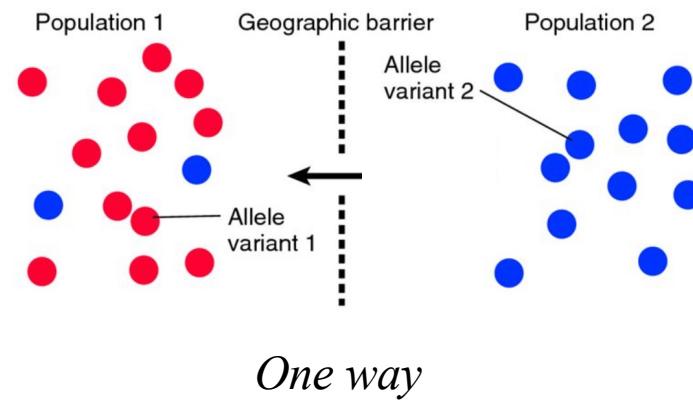
# Factors Influencing Allele Frequencies

- *Mutation*
- **Migration**
- *Genetic Drift*
- *Natural Selection*



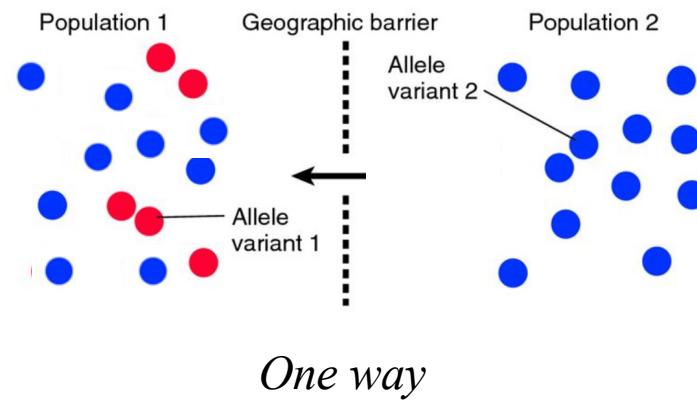
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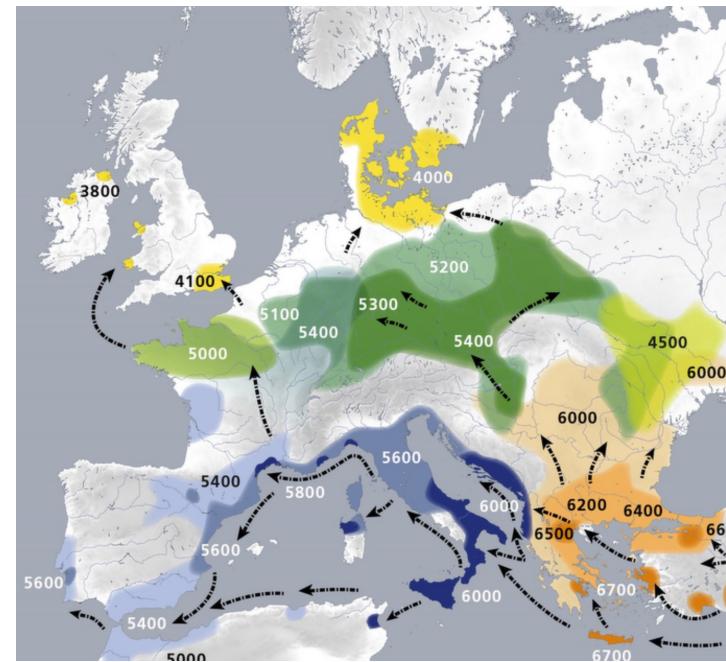
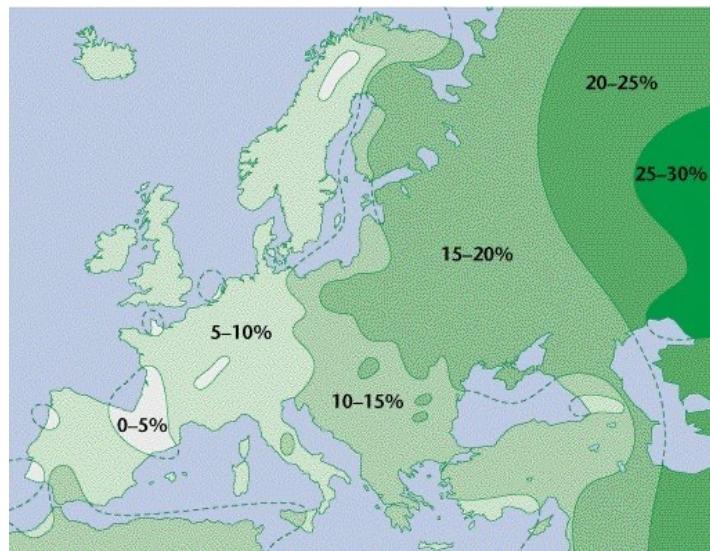
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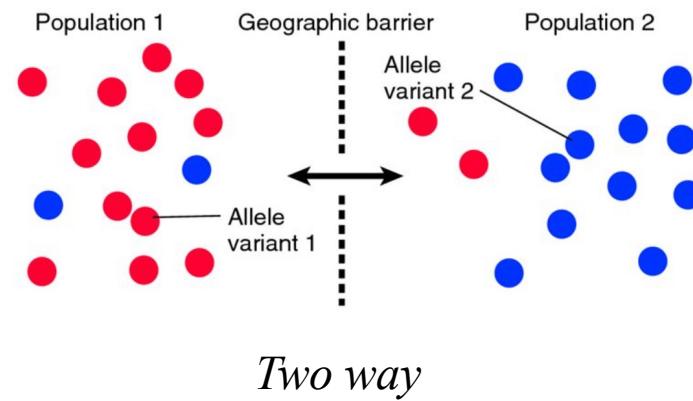
Migration patterns can help explain spatial variation in the frequency of the *B* allele

*Frequency of the B blood type across a geographical region*



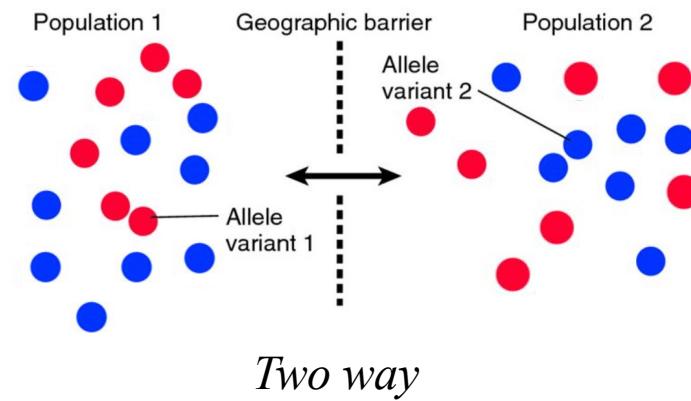
# Factors Influencing Allele Frequencies

- *Mutation*
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# Factors Influencing Allele Frequencies

- *Mutation*
- **Migration**
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- *Natural Selection*



## Migration as a force changing allele frequencies can be opposed by selection



Volcanic soil



shutterstock.com · 1555712840



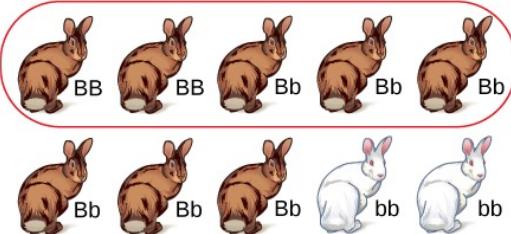
# Factors Influencing Allele Frequencies

- *Mutation*
- *Migration*
- *Genetic Drift*
- *Natural Selection*

# Genetic Drift

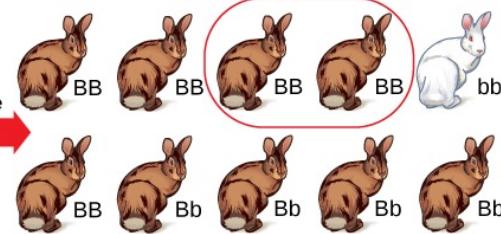
## First generation

p (B gene frequency) = .5  
q (b gene frequency) = .5



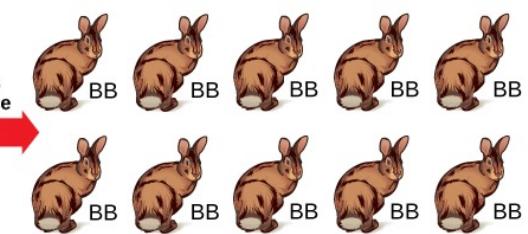
## Second generation

p = .7  
q = .3

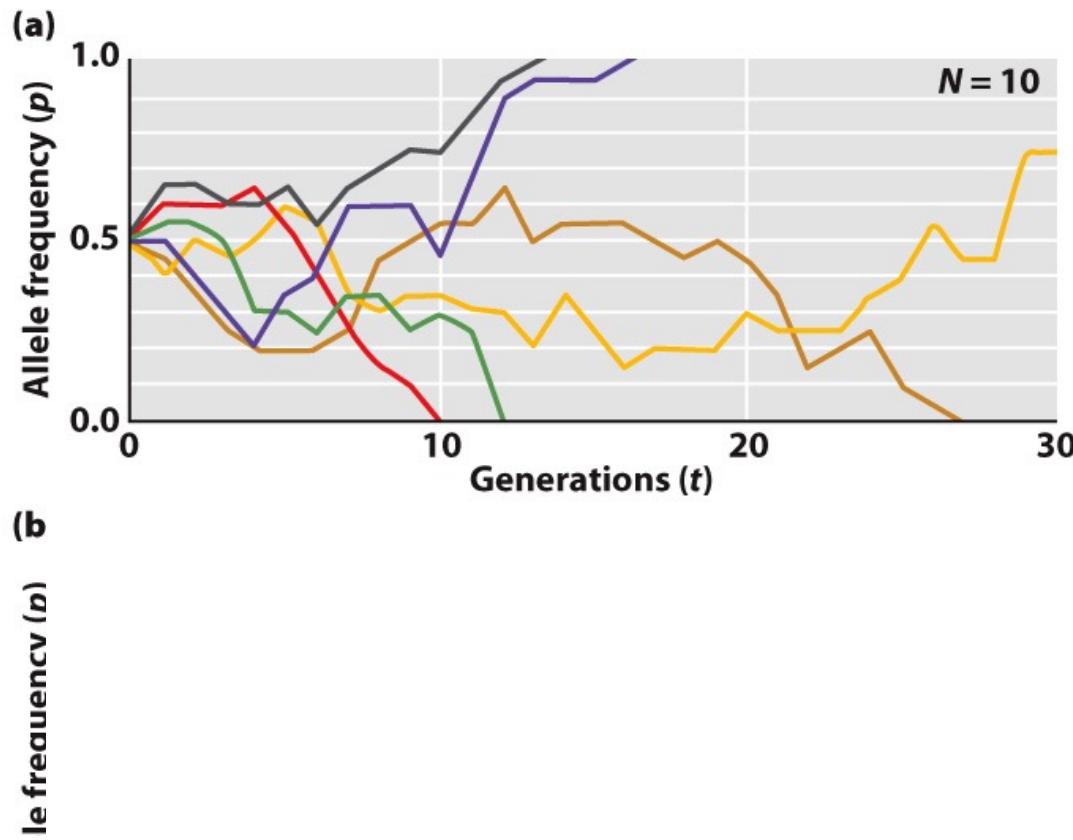


## Third generation

p = 1  
q = 0

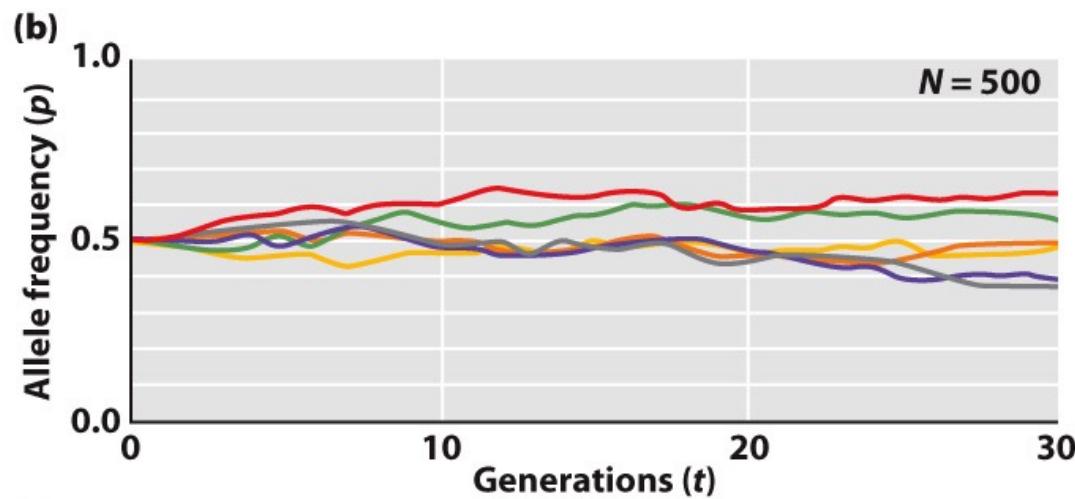


## Random genetic drift is strong in small populations



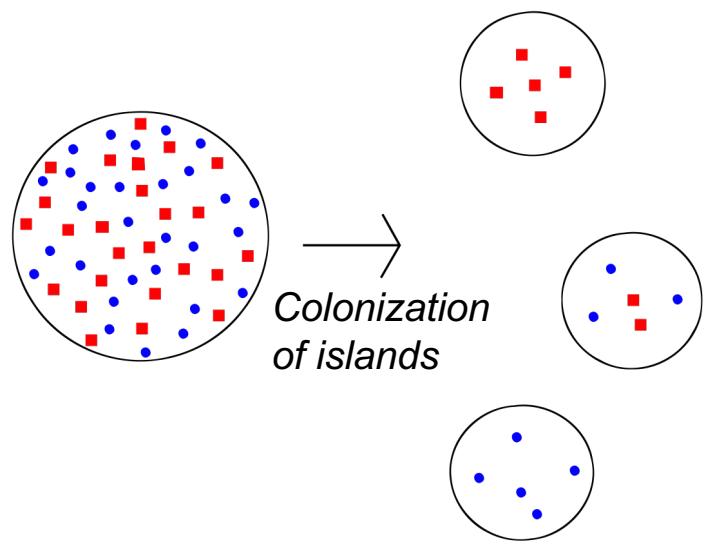
*Each colour represents the frequency of one of the alleles at a biallelic locus*

Random genetic drift is weaker in large populations



*Each colour represents the frequency of one of the alleles at a biallelic locus*

## Genetic Drift (and population “bottlenecks”)

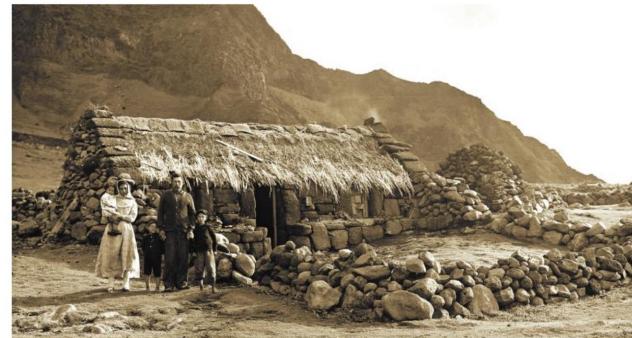


*Founding events*

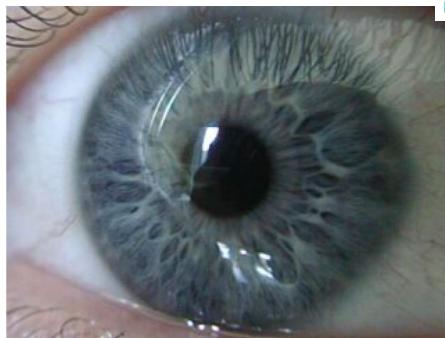
## Genetic Drift: High frequency of Retinitis pigmentosa in the Inhabitants of Tristan da Cuhna



The Founder Effect is Another Variation of Genetic Drift

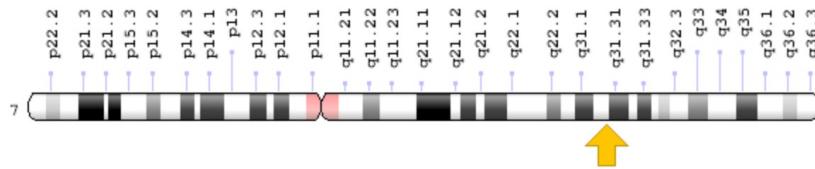


The South Atlantic island of Tristan da Cunha was colonized by 15 Britains in 1814, one of them carrying an allele for retinitis pigmentosum. Among

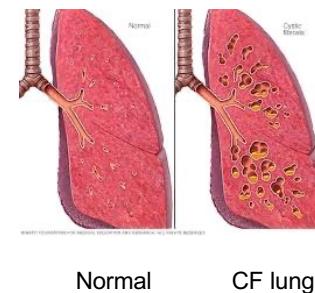


# Genetic Drift (CF)

Average Cystic Fibrosis incidence worldwide (1 out of 2,500),  
but in Saguenay region of Quebec (1 out of 936)



CFTR gene is on Chromosome 7

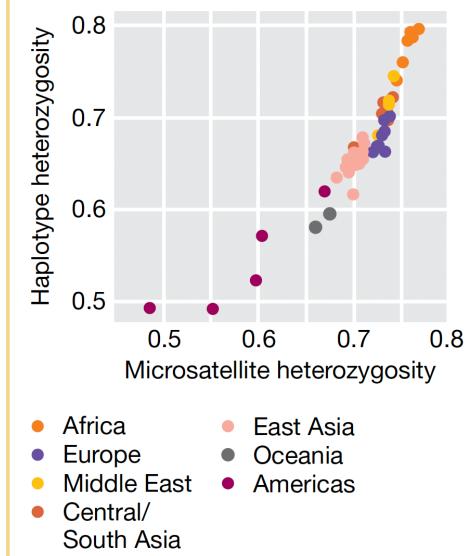


# Genetic Drift (and “founding events”)

Figure 1: Human migration out of Africa.



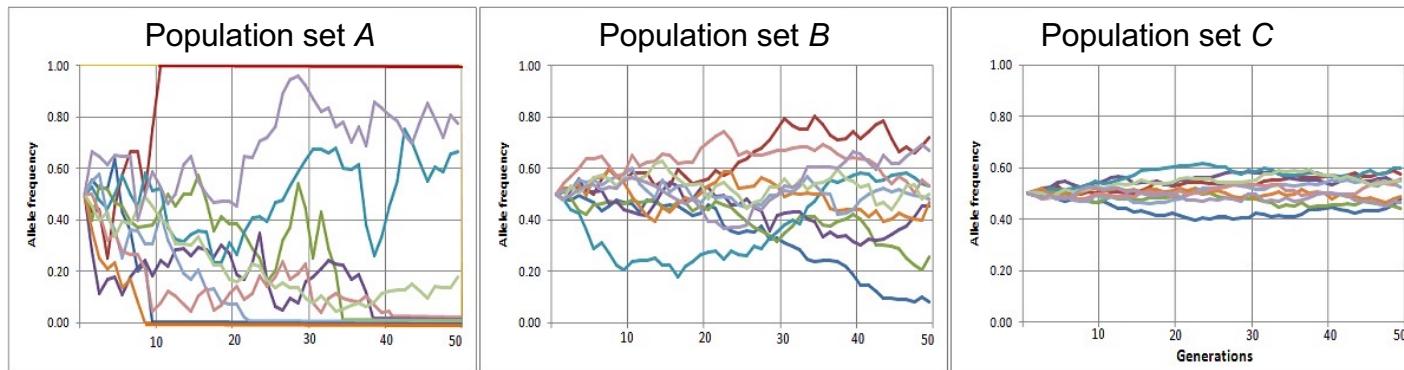
Human populations have different levels of genetic diversity



# Factors Influencing Allele Frequencies in Populations

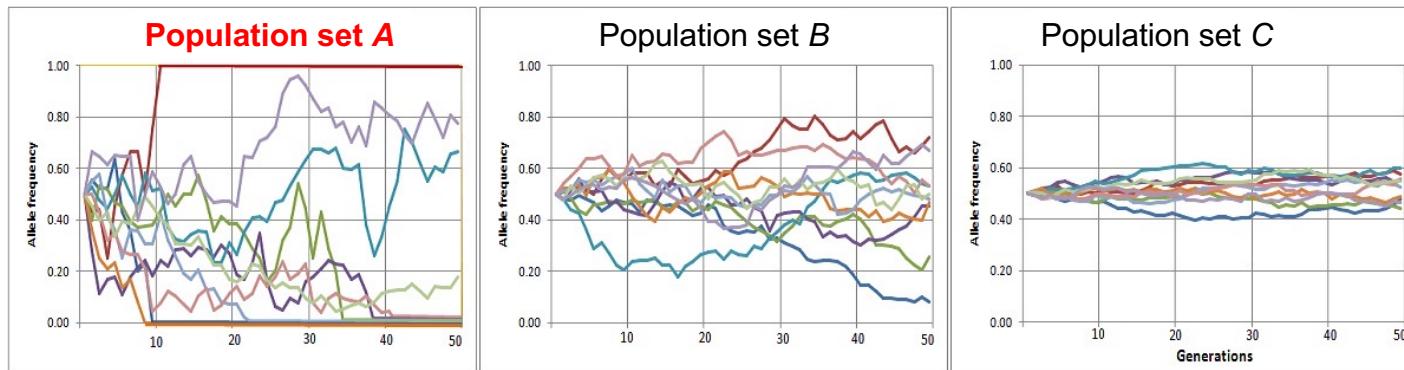
- *Mutation*
- *Migration*
- *Genetic Drift*
- *Natural Selection (next time)*

For the allele frequency\* versus time graphs shown below, which population set is likely the smallest in size?



\*Each colour represents the frequency of alleles at a different biallelic locus

For the allele frequency\* versus time graphs shown below, which population set is likely the smallest in size?



\*Each colour represents the frequency of alleles at a different biallelic locus

## Lecture 11 (Main points)

- Inbreeding increases the probability of identity by descent, and in so doing, the probability of homozygosity.
- Inbreeding depression can occur when deleterious, recessive alleles are homozygous.
- Mutation is the ultimate source of genetic variation, but occurs rarely at a single locus, and thus does not alter allele or genotype frequencies rapidly.
- Migration can be frequent or infrequent. When frequent and non-directional it tends to homogenize the allele and genotype frequencies of separate populations. Migration can be maladaptive.
- Genetic drift moves allele frequencies up or down with equal probability. It is strongest in small populations.