

# Population Genomics 101: Population Size, Genetic Drift, and Inbreeding

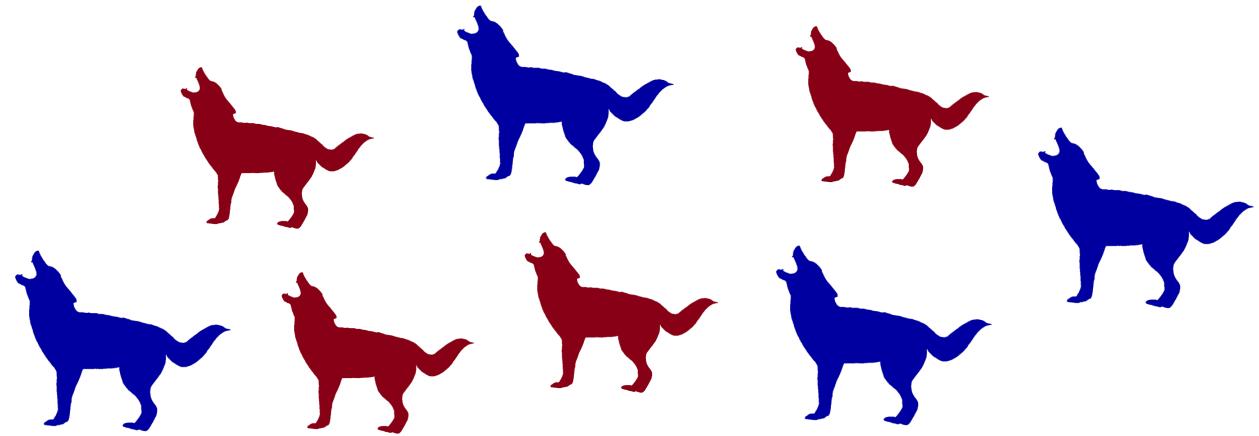


Alexander Ochoa | GDW 2023

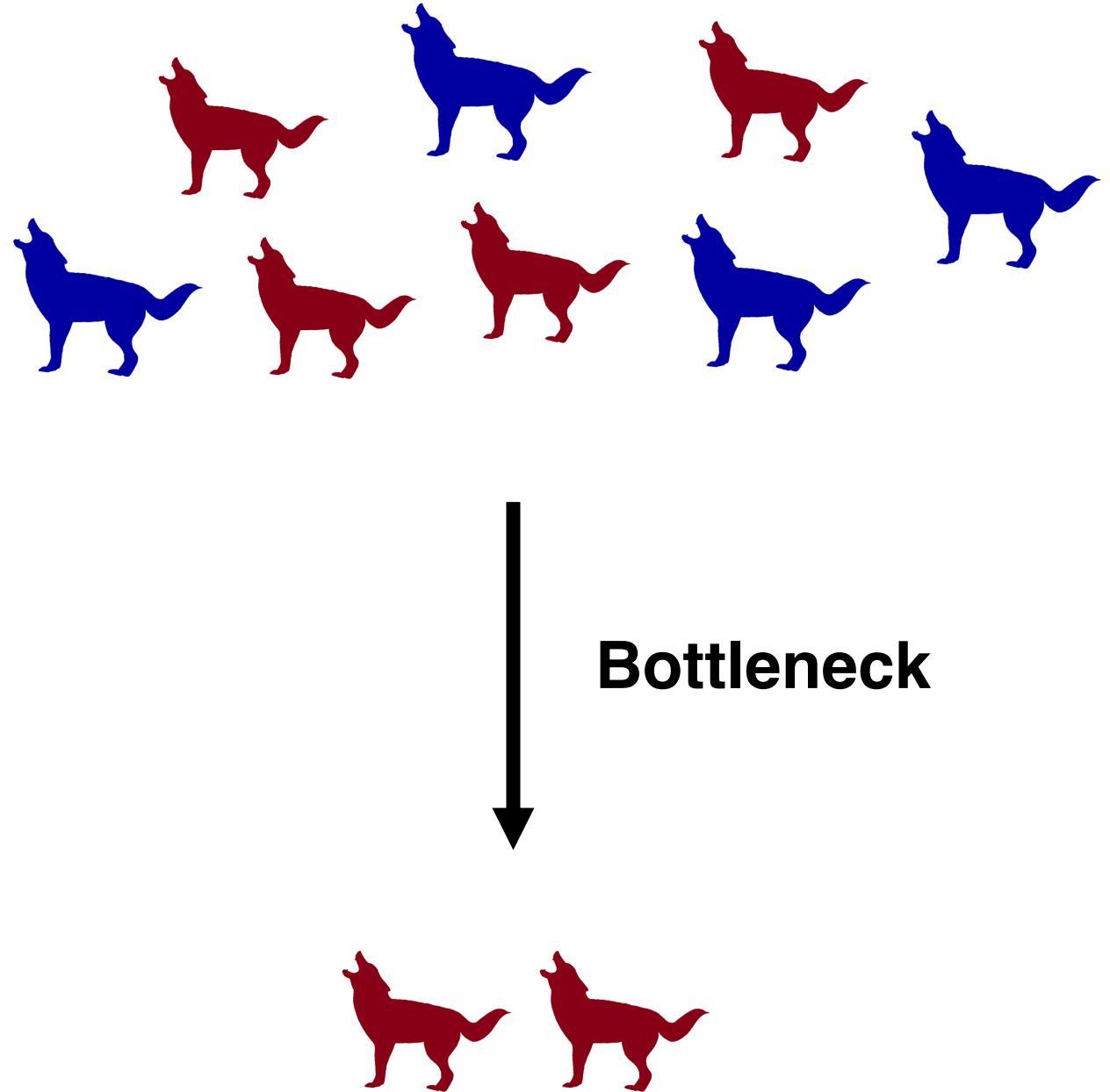
# Extinction Vortex



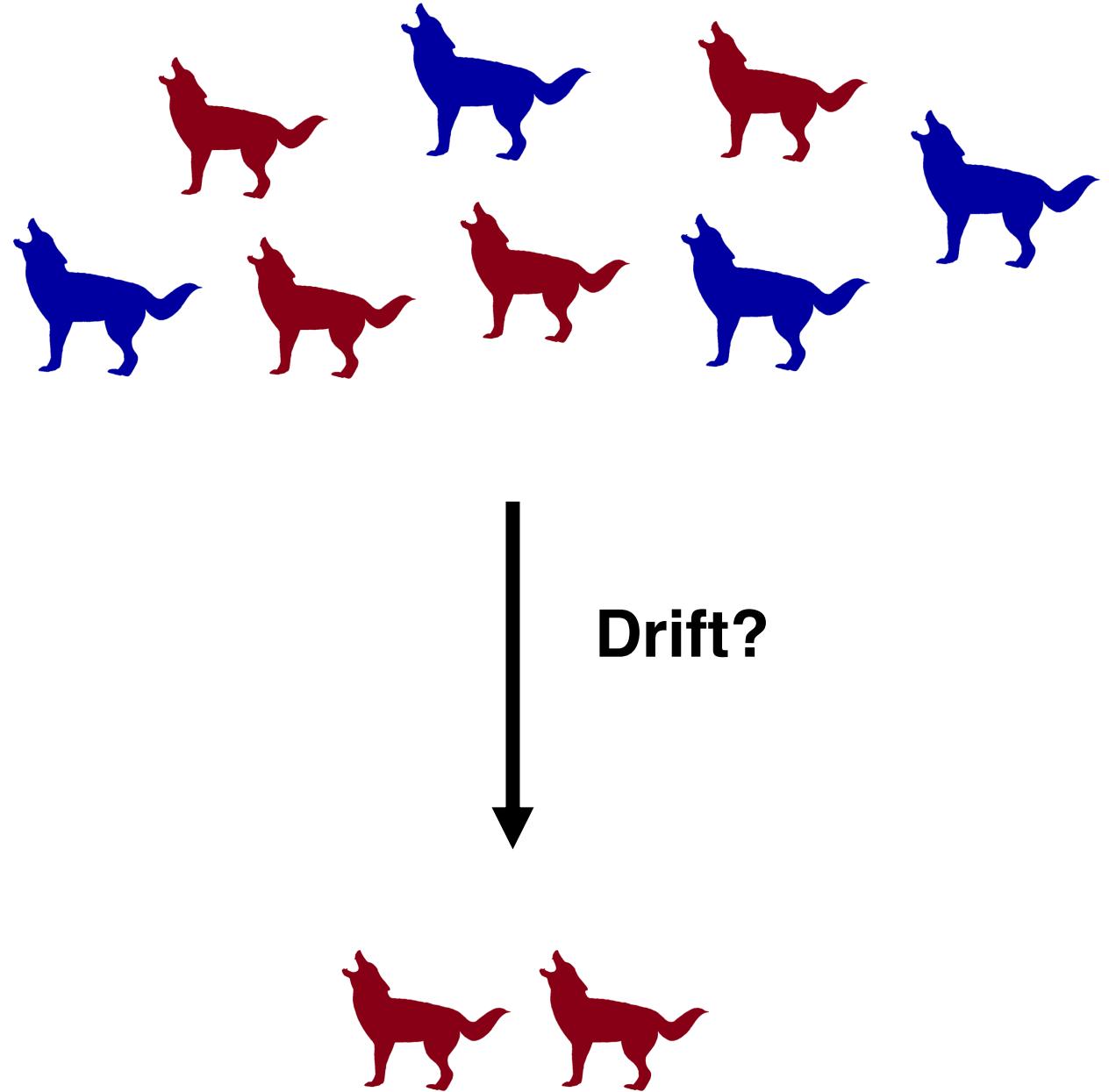
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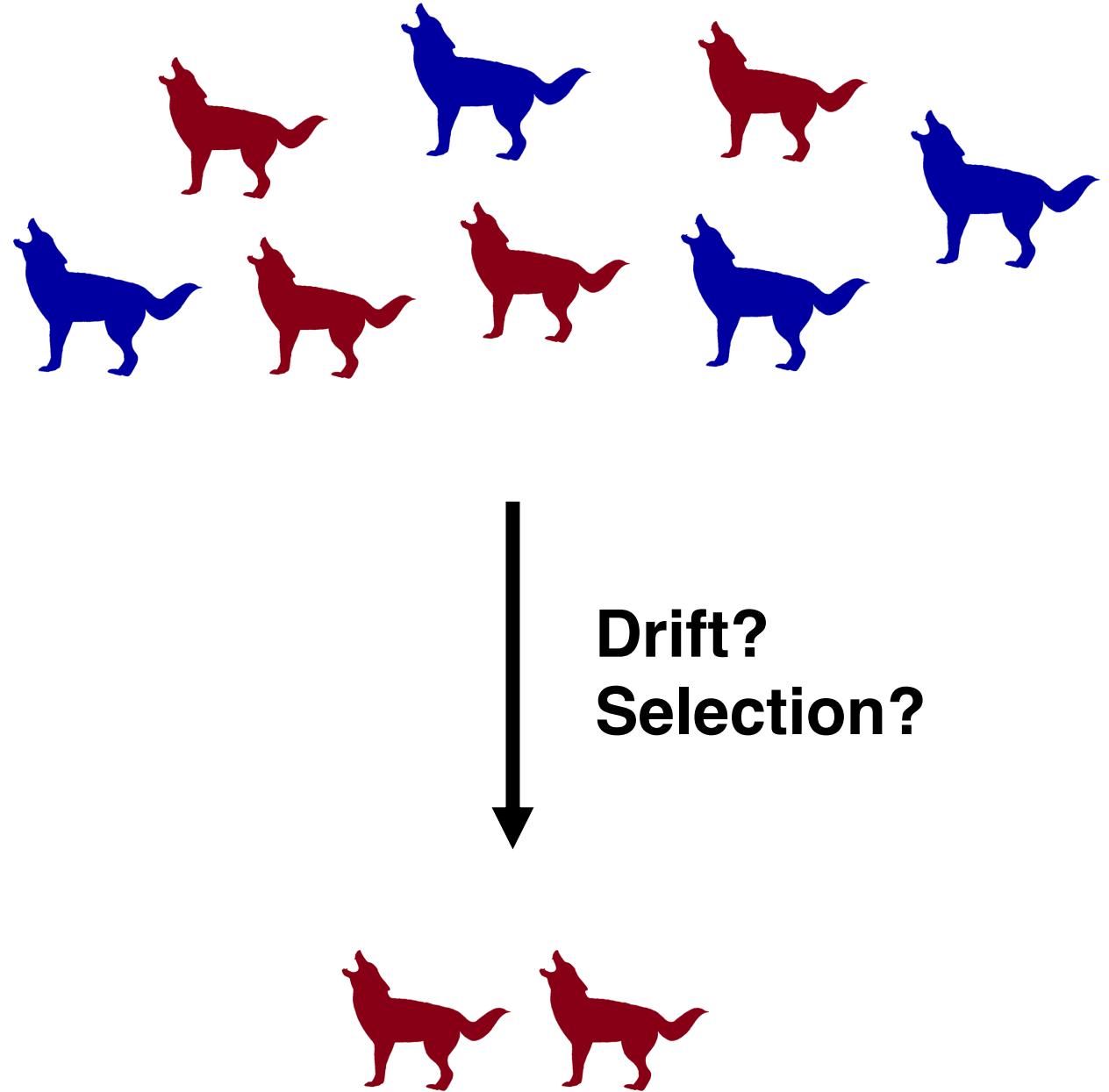
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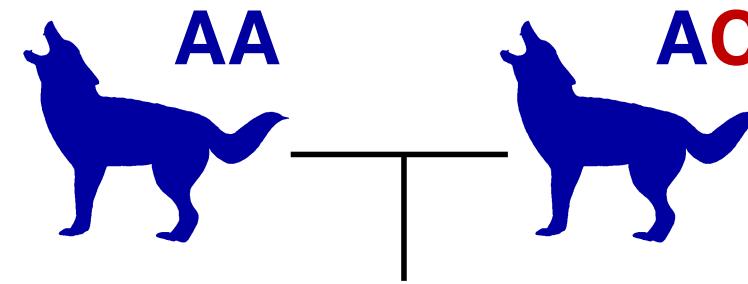


# Inbreeding

# Extinction Vortex



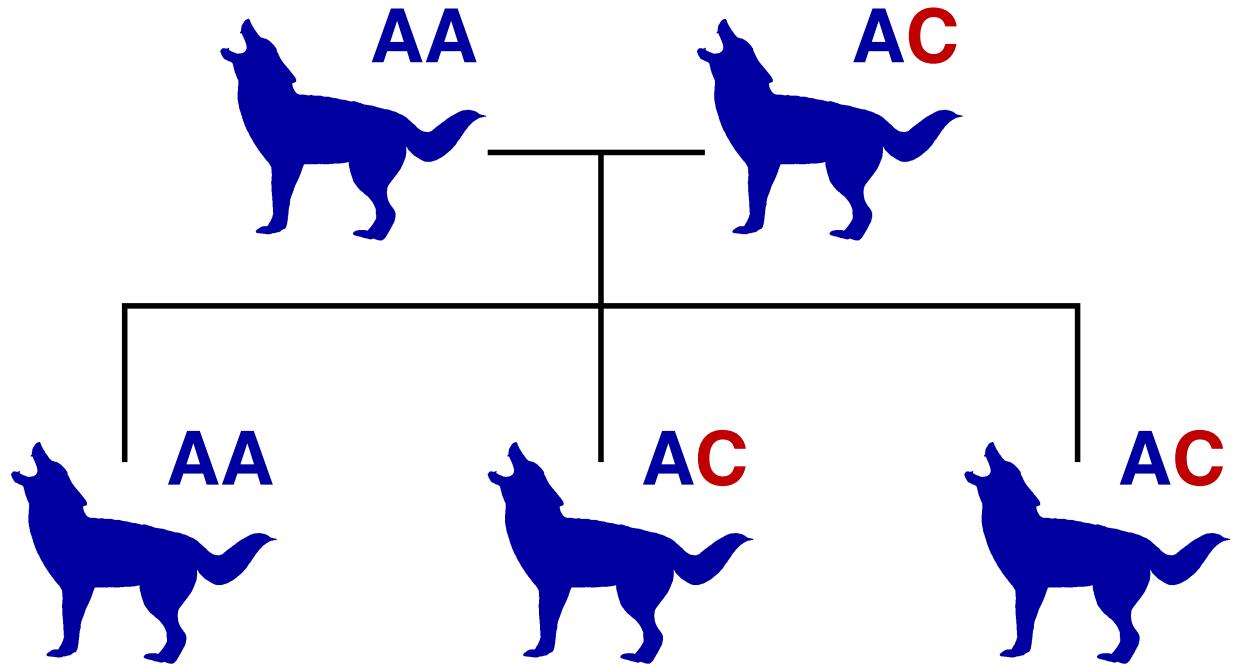
# Inbreeding



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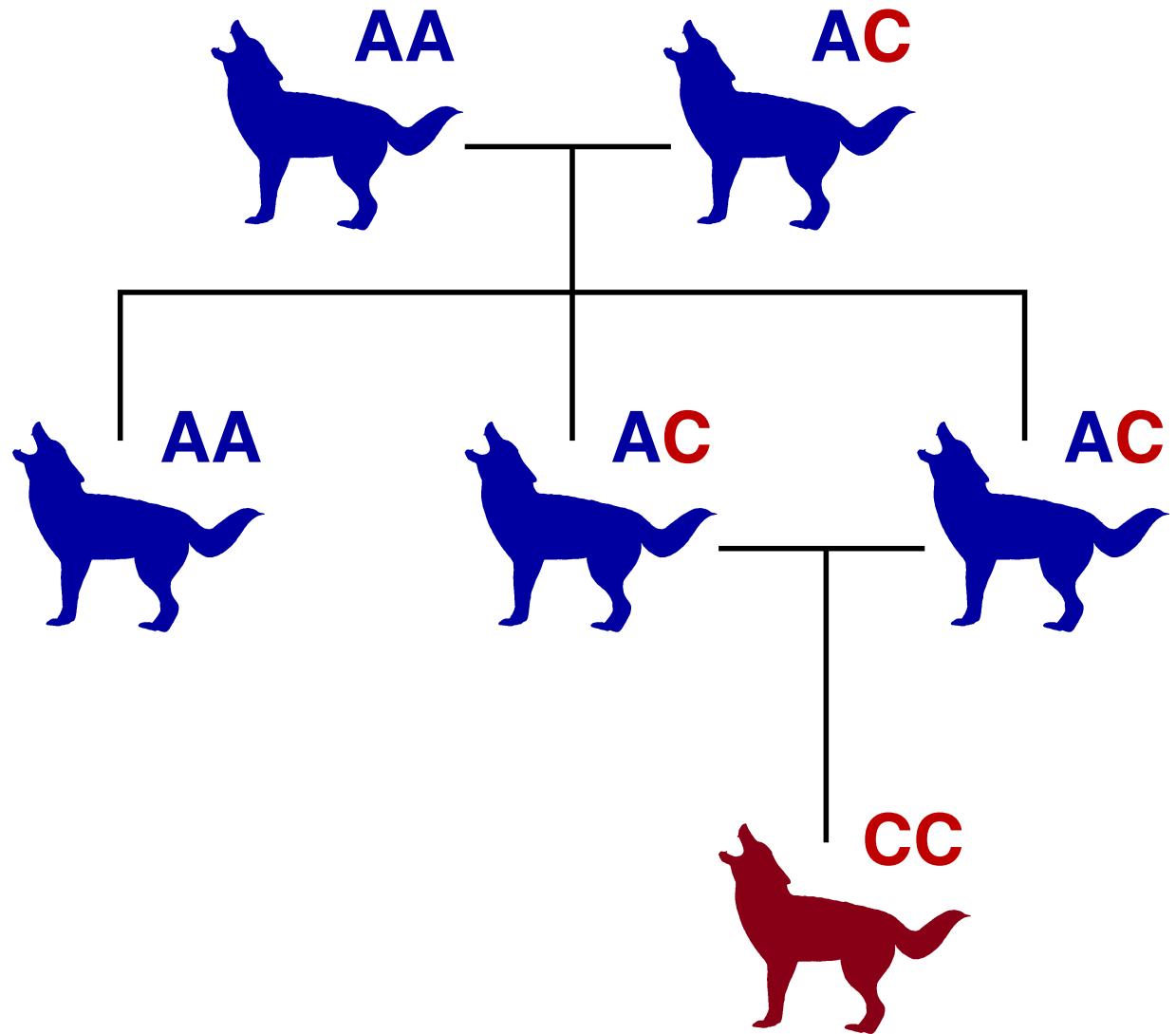
# Inbreeding



# Extinction Vortex



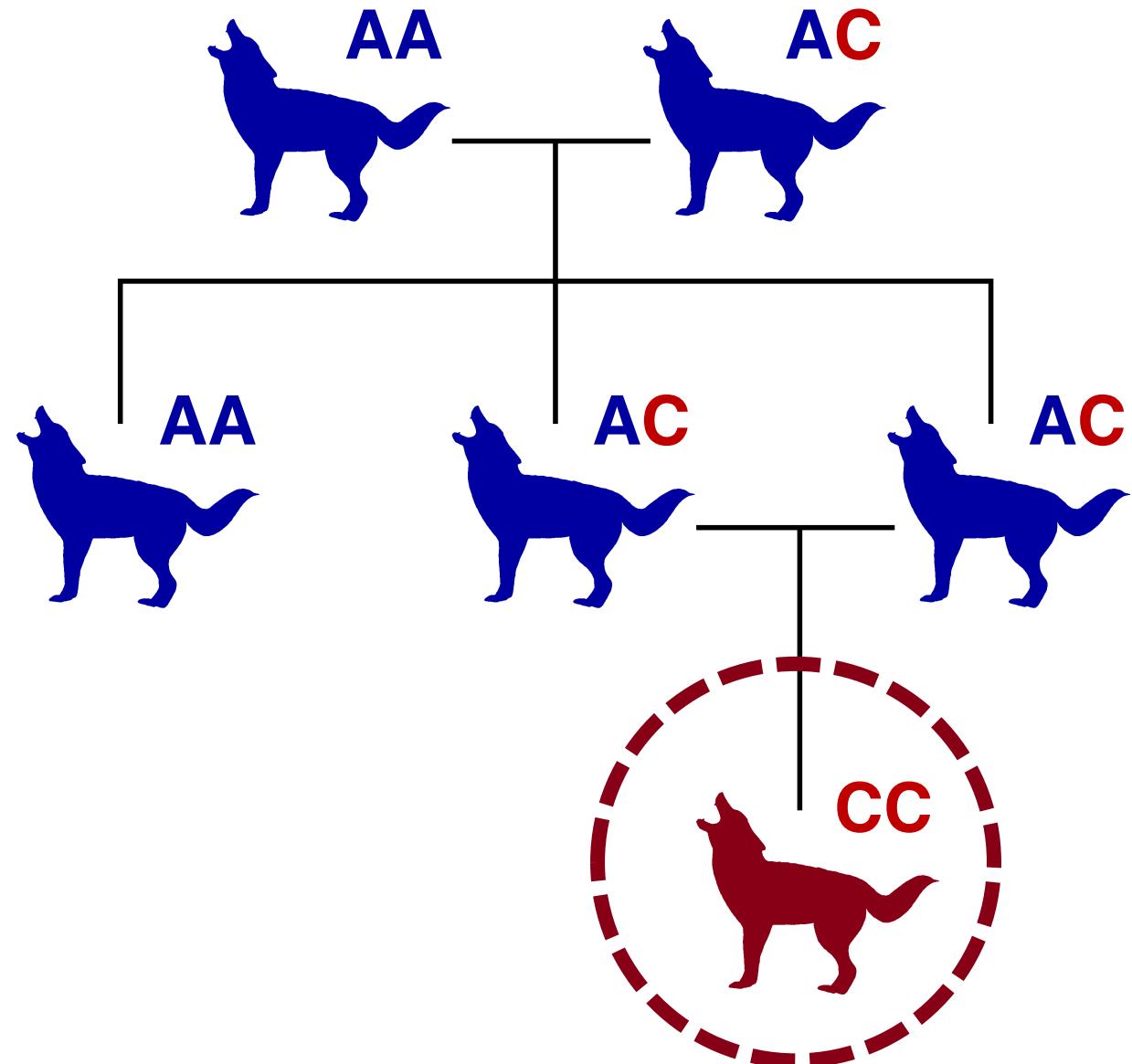
# Inbreeding



# Extinction Vortex



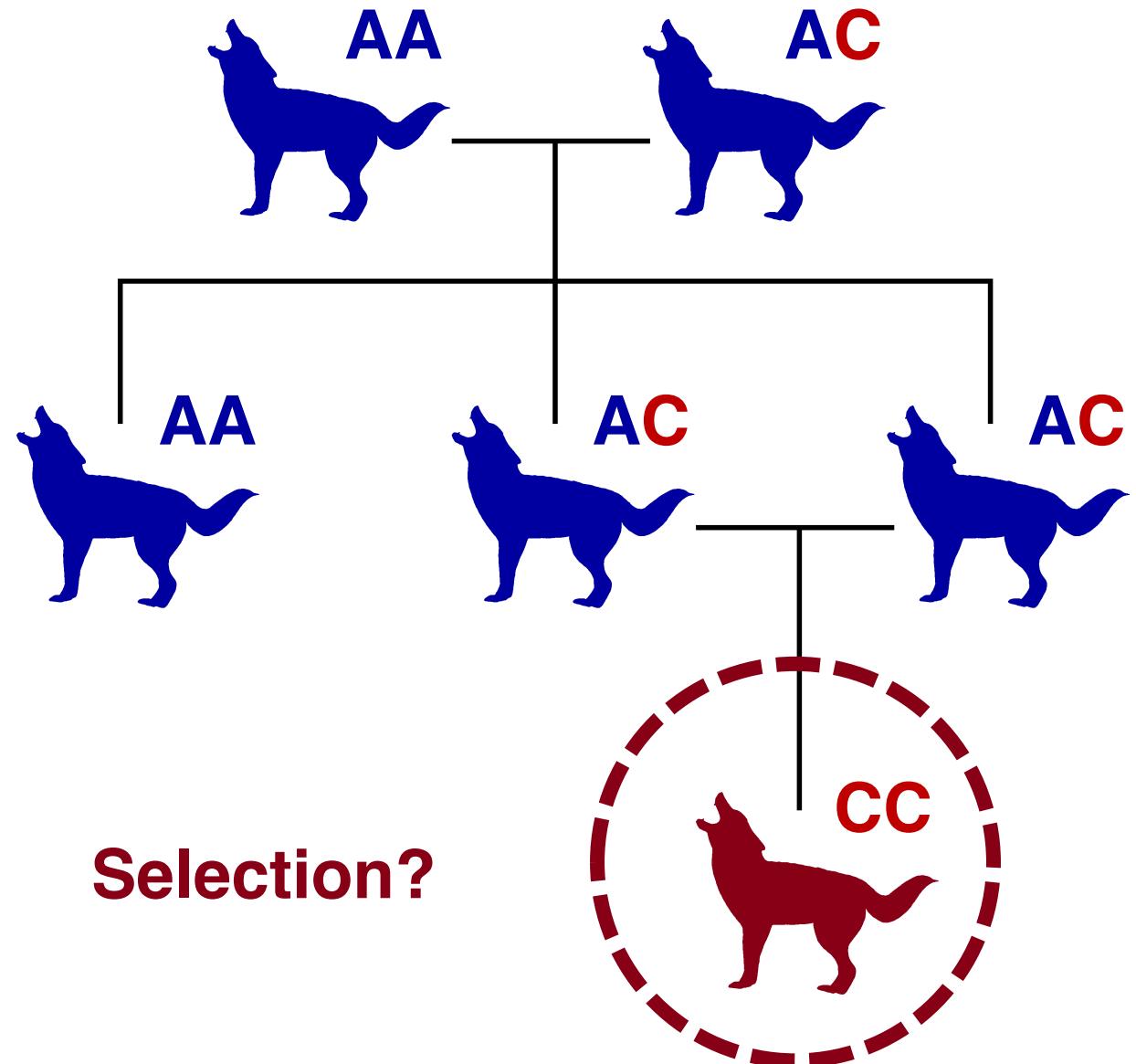
# Inbreeding Depression?



# Extinction Vortex



# Inbreeding Depression?

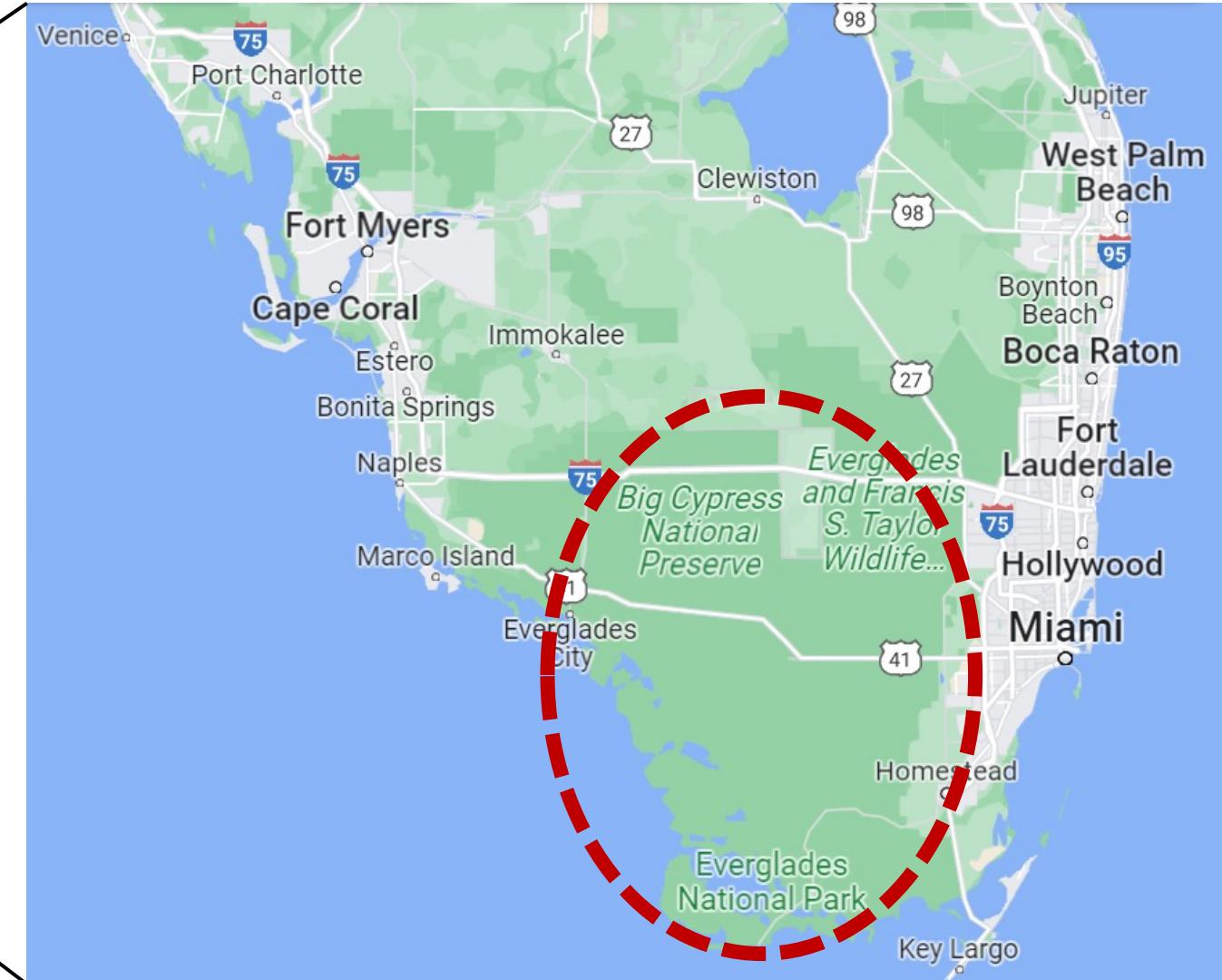
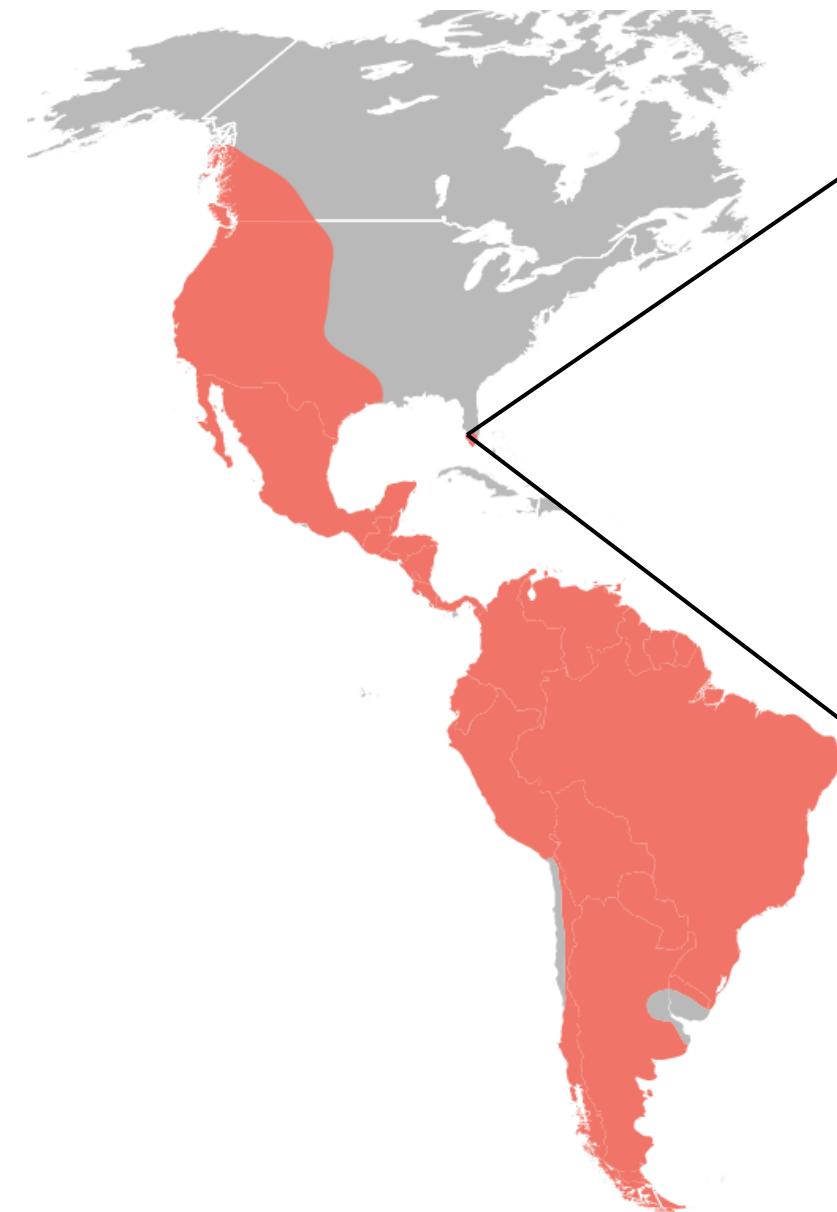




## Florida panthers:

- Low genetic variation
- High inbreeding
- High disease rate

# Florida Panthers: Distribution



# Florida Panthers: Inbreeding



Thoracic cowlicks



Kinked tails

# Florida Panthers: Inbreeding Depression

- Spermatozoal defects
- Low testosterone
- **Cryptorchidism**
- Cardiac defects
- Susceptibility to diseases

# Florida Panthers: Genetic Rescue



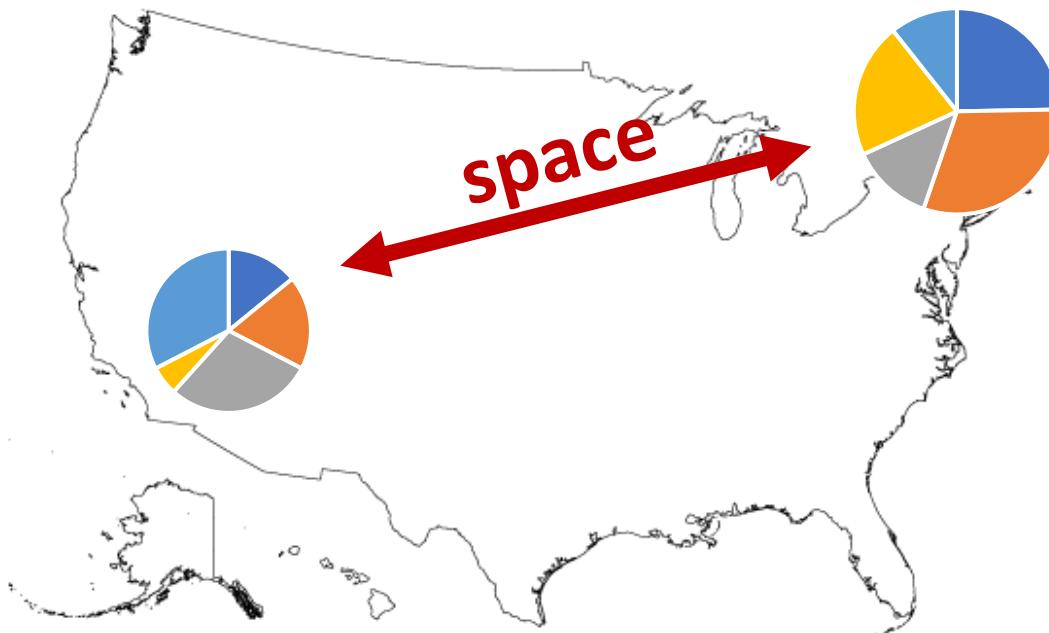
# Population Genetics

- Study of genetic variation within and between populations  
**AND** the different factors shaping that variation

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- Study of genetic variation within and between populations  
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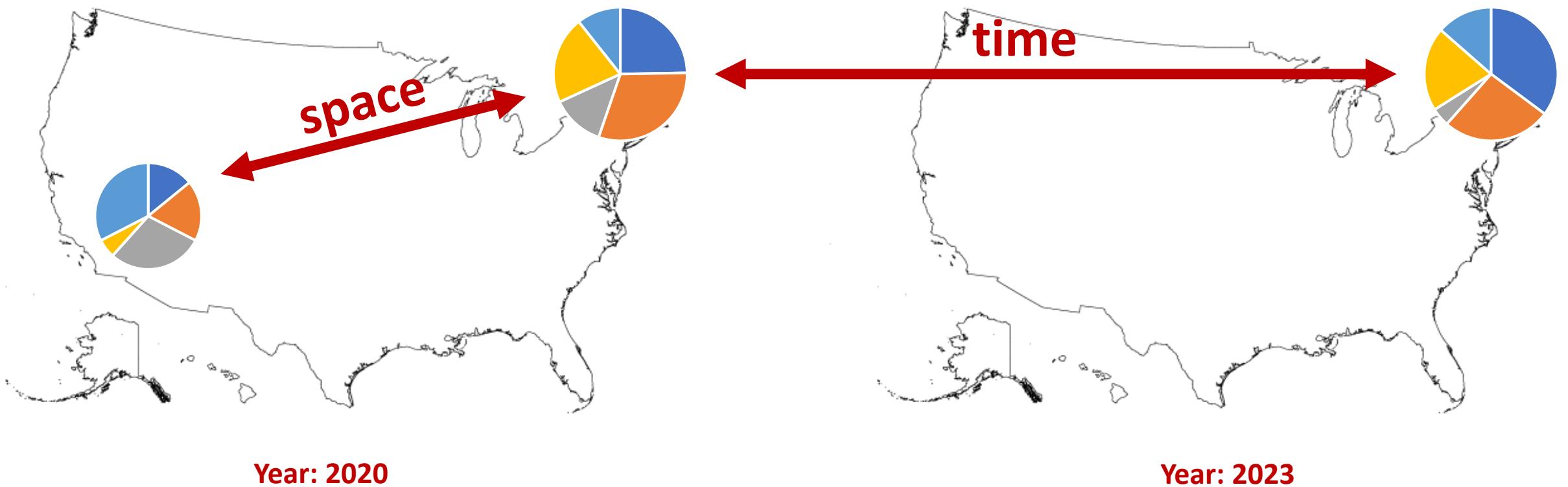


Year: 2020

# Population Genetics



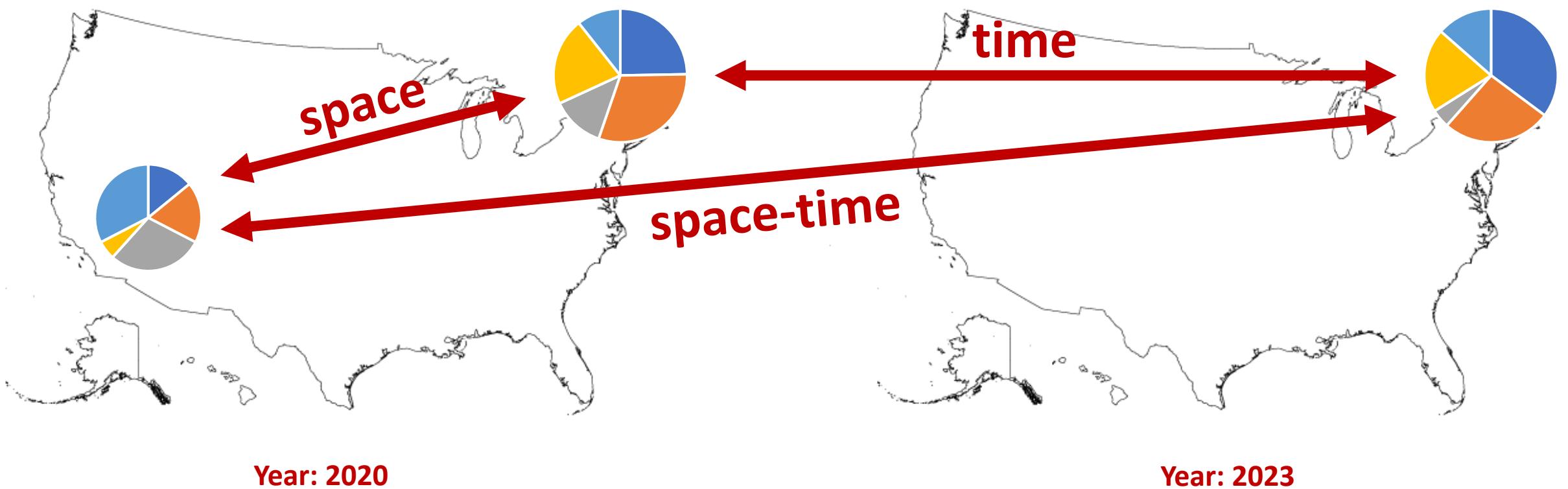
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**AND** the different factors shaping that variation



# Population Genetics



- Study of genetic variation within and between populations  
**AND** the different factors shaping that variation



# **Population Genetics**

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**AND** the different factors shaping that variation

# **Population Genomics?**

# **Population Genetics**

- Study of genetic variation within and between populations  
**AND** the different factors shaping that variation

# **Population Genomics?**

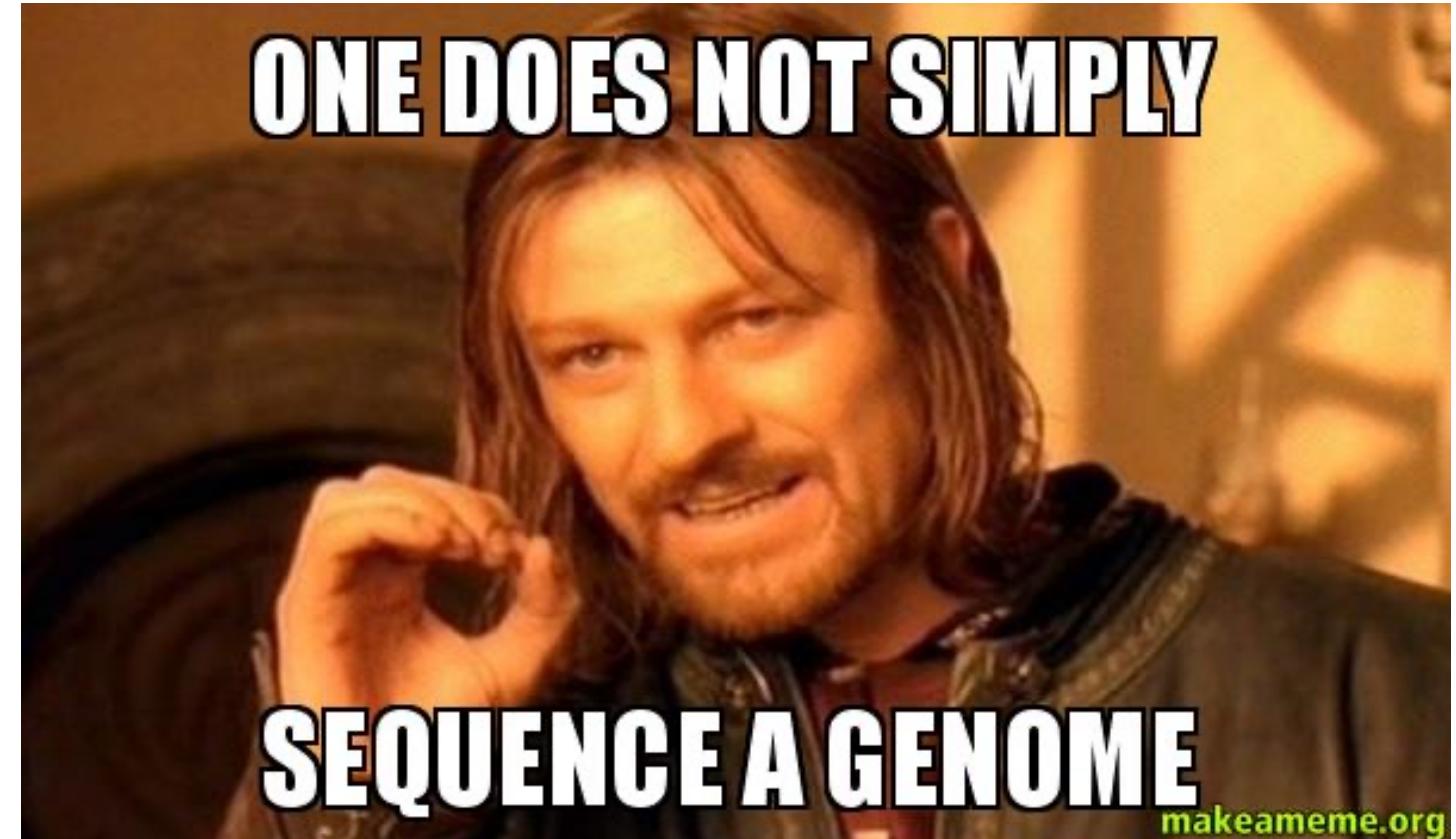
- Population genetics at  
the genome-wide scale

# Population Genetics

- Study of genetic variation within and between populations  
**AND** the different factors shaping that variation

## Population Genomics?

- Population genetics at the genome-wide scale



# Hardy-Weinberg Principle

- Genetic variation in a population remains constant from one generation to the next one
- Null model of evolution assuming a random mating scheme
- Significant deviations from Hardy-Weinberg expectations indicate populations are evolving and/or their individuals are not mating randomly

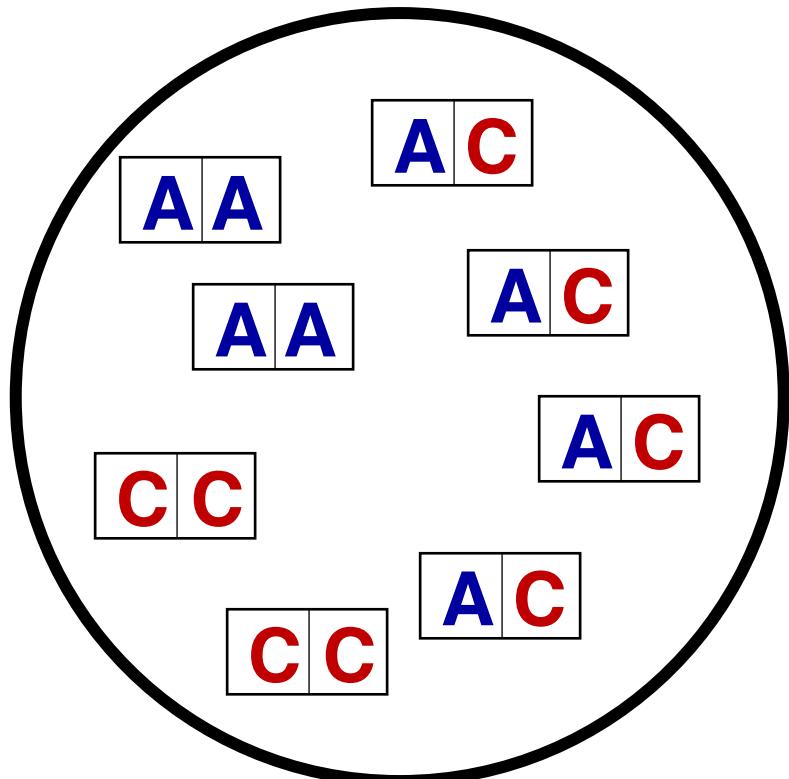
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# Hardy-Weinberg Equilibrium

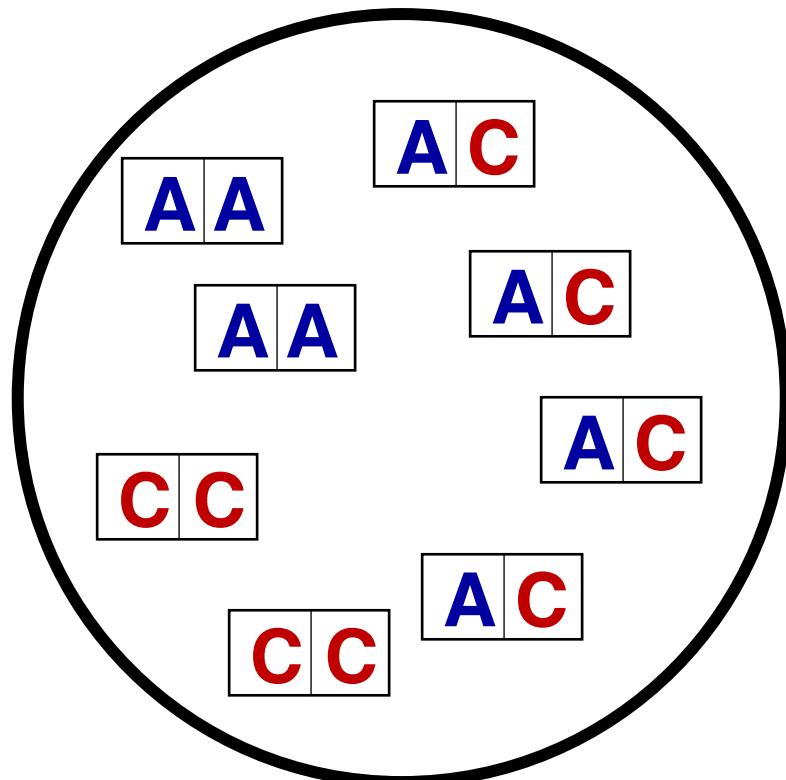


Chrom 1, Position 328

# Hardy-Weinberg Equilibrium

Freq A ( $p$ ) = 0.5

Freq C ( $q$ ) = 0.5

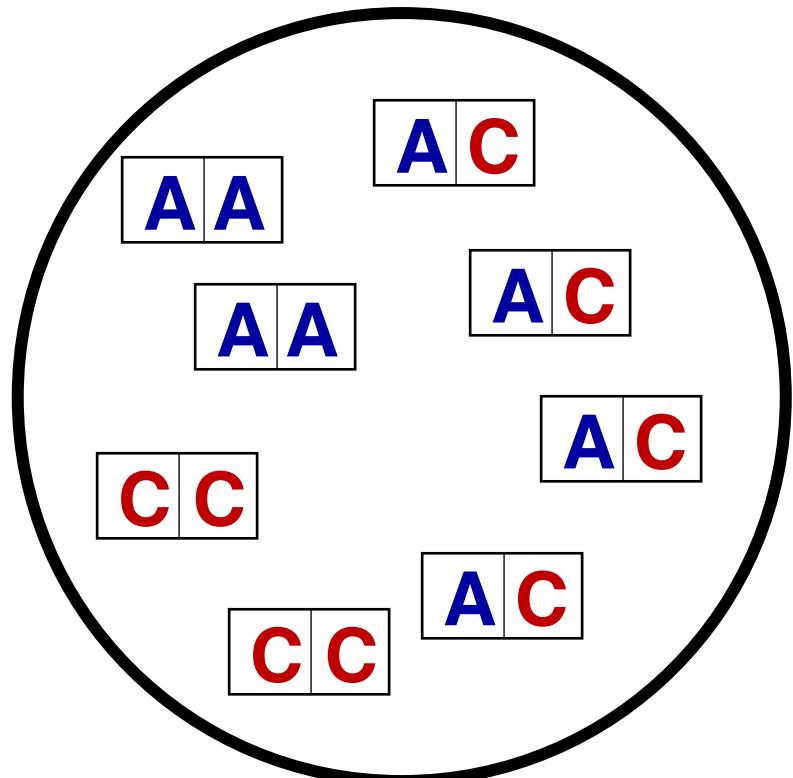


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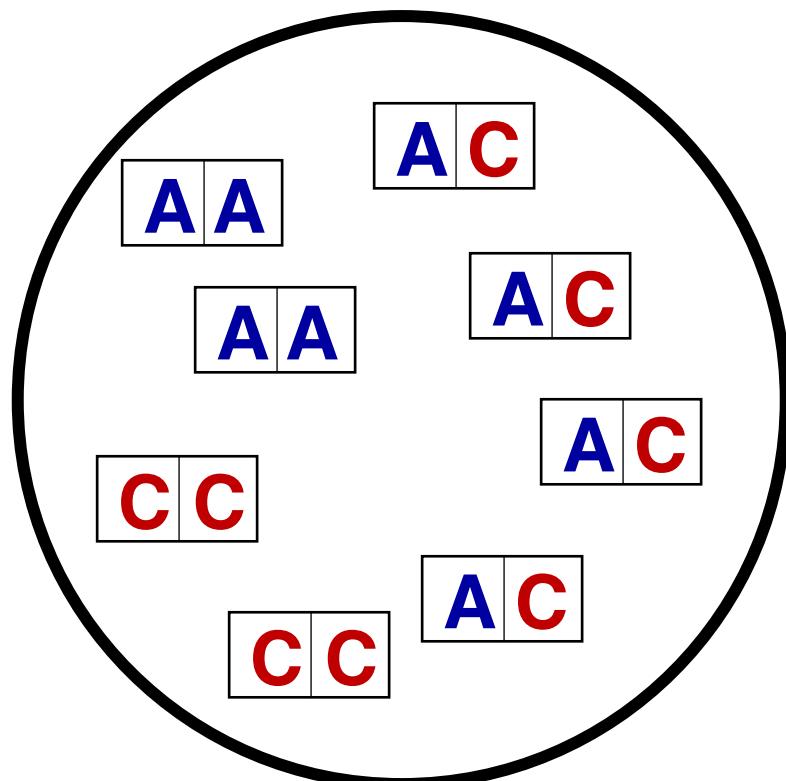
$$p^2 + 2pq + q^2 = 1$$

Chrom 1, Position 328

# Hardy-Weinberg Equilibrium

Freq A ( $p$ ) = 0.5

Freq C ( $q$ ) = 0.5



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

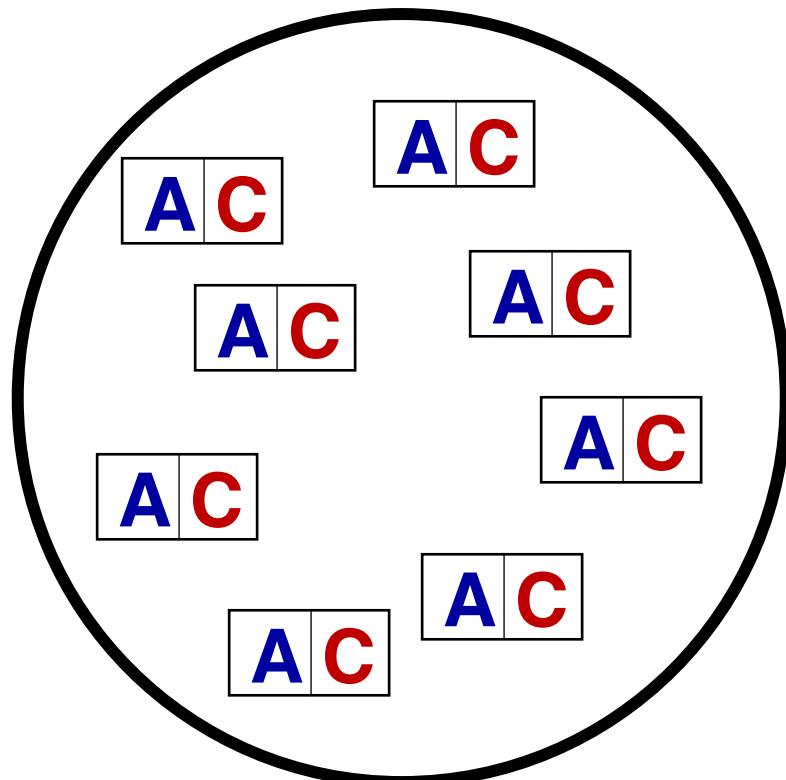
Homozygotes ( $p^2$ ) = 0.25  
Heterozygotes ( $2pq$ ) = 0.5  
Homozygotes ( $q^2$ ) = 0.25

Chrom 1, Position 328

# NOT in Hardy-Weinberg Equilibrium

Freq A ( $p$ ) = 0.5

Freq C ( $q$ ) = 0.5



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

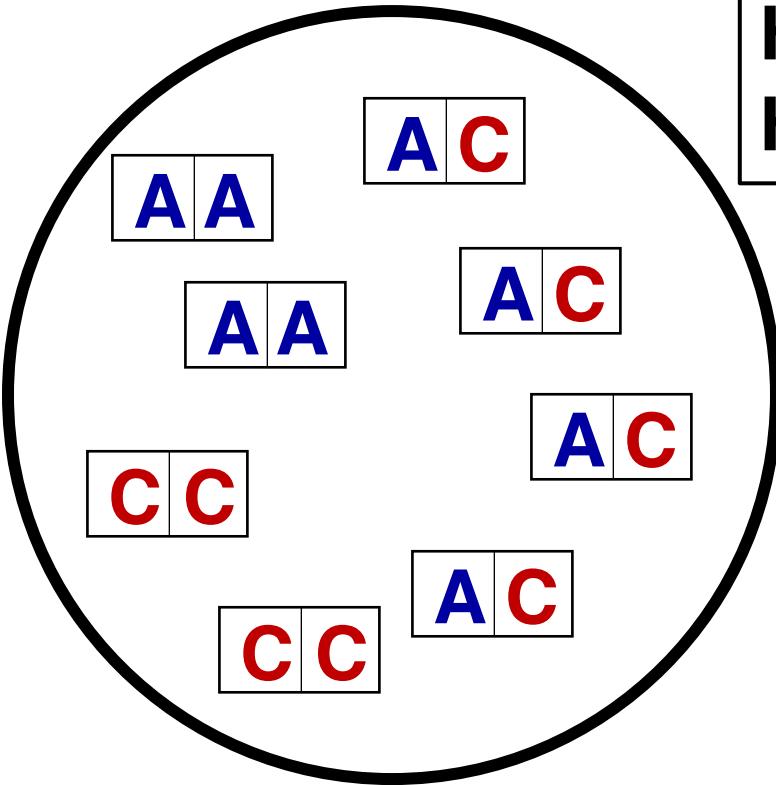
Homozygotes ( $p^2$ ) = 0.25  
Heterozygotes ( $2pq$ ) = 0.5  
Homozygotes ( $q^2$ ) = 0.25

Chrom 1, Position 685

# Evolving Populations

Freq A ( $p$ ) = 0.5

Freq C ( $q$ ) = 0.5



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

Homozygotes ( $p^2$ ) = 0.25

Heterozygotes ( $2pq$ ) = 0.5

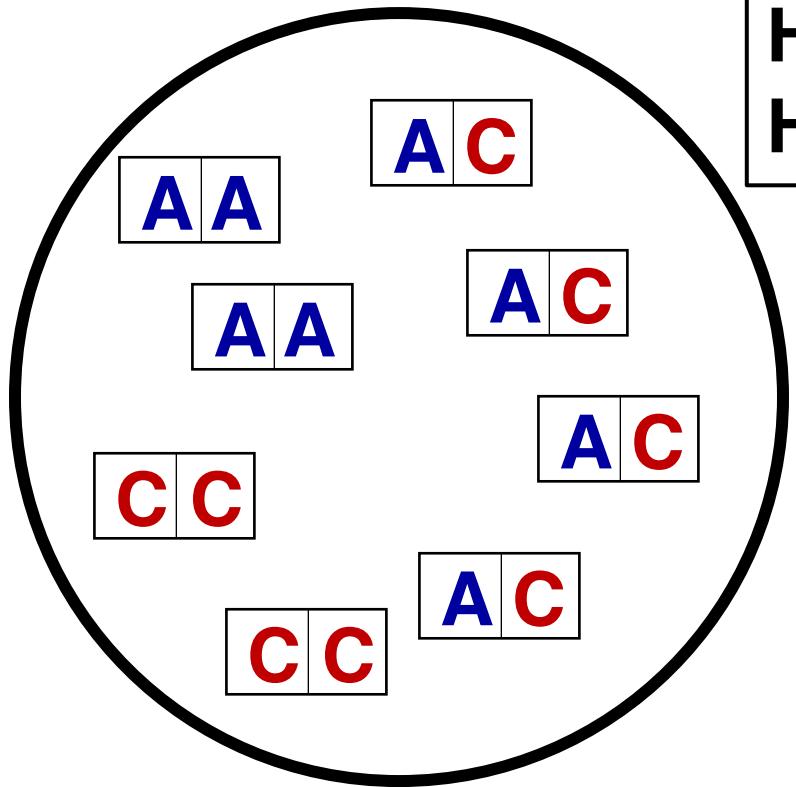
Homozygotes ( $q^2$ ) = 0.25

Generation 0

# Evolving Populations

Freq A ( $p$ ) = 0.5

Freq C ( $q$ ) = 0.5

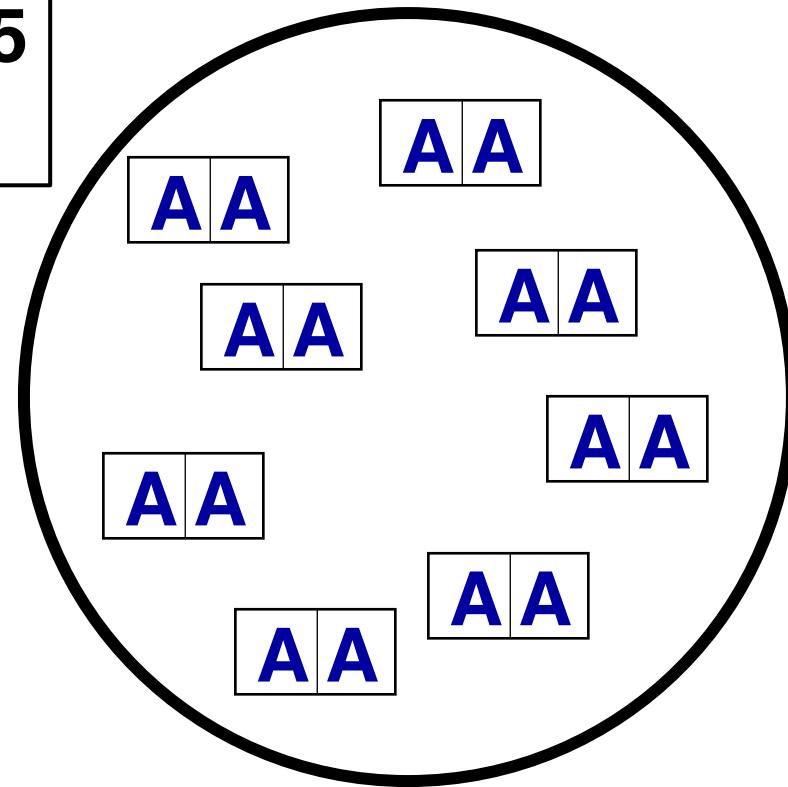


$$p^2 + 2pq + q^2 = 1$$

Homozygotes ( $p^2$ ) = 0.25  
Heterozygotes ( $2pq$ ) = 0.5  
Homozygotes ( $q^2$ ) = 0.25

Freq A ( $p$ ) = 1

Freq C ( $q$ ) = 0



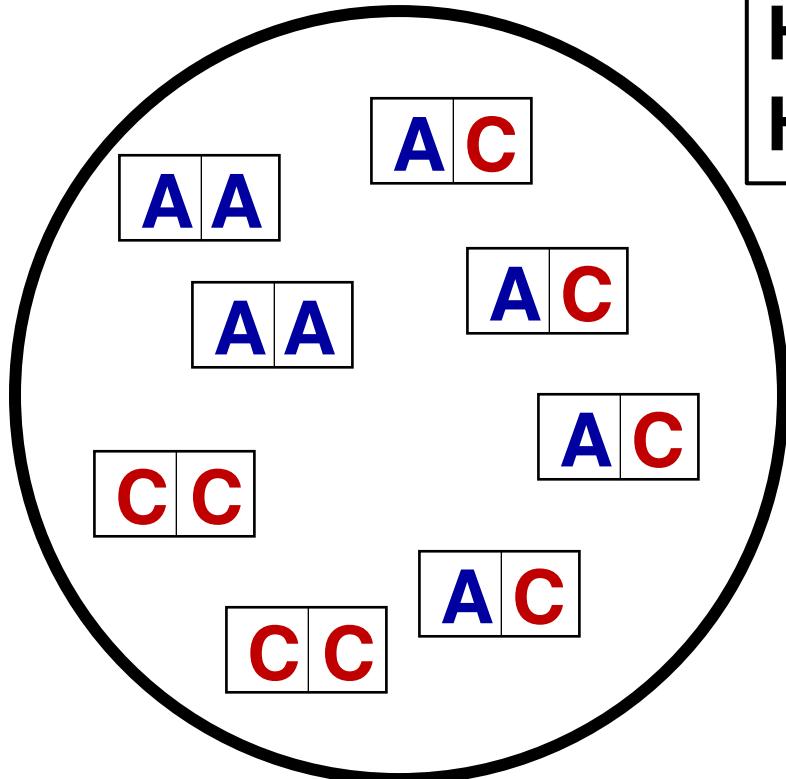
Generation 0

Generation 1

# Evolving Populations

Freq A ( $p$ ) = 0.5

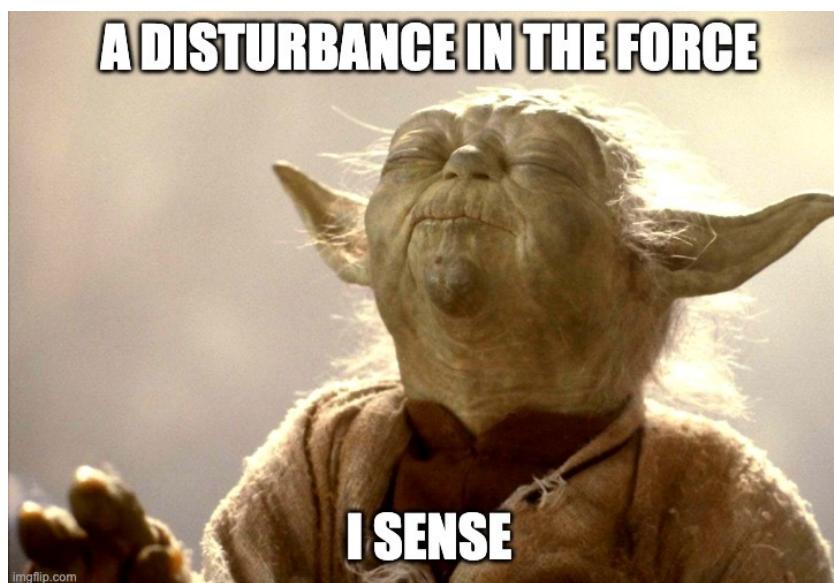
Freq C ( $q$ ) = 0.5



Generation 0

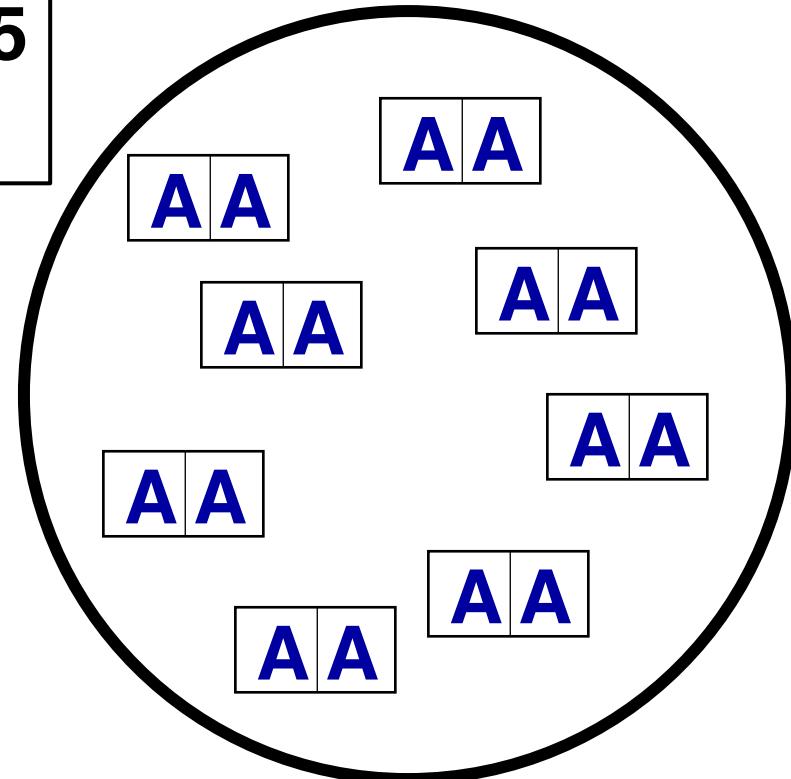
$$p^2 + 2pq + q^2 = 1$$

Homozygotes ( $p^2$ ) = 0.25  
Heterozygotes ( $2pq$ ) = 0.5  
Homozygotes ( $q^2$ ) = 0.25



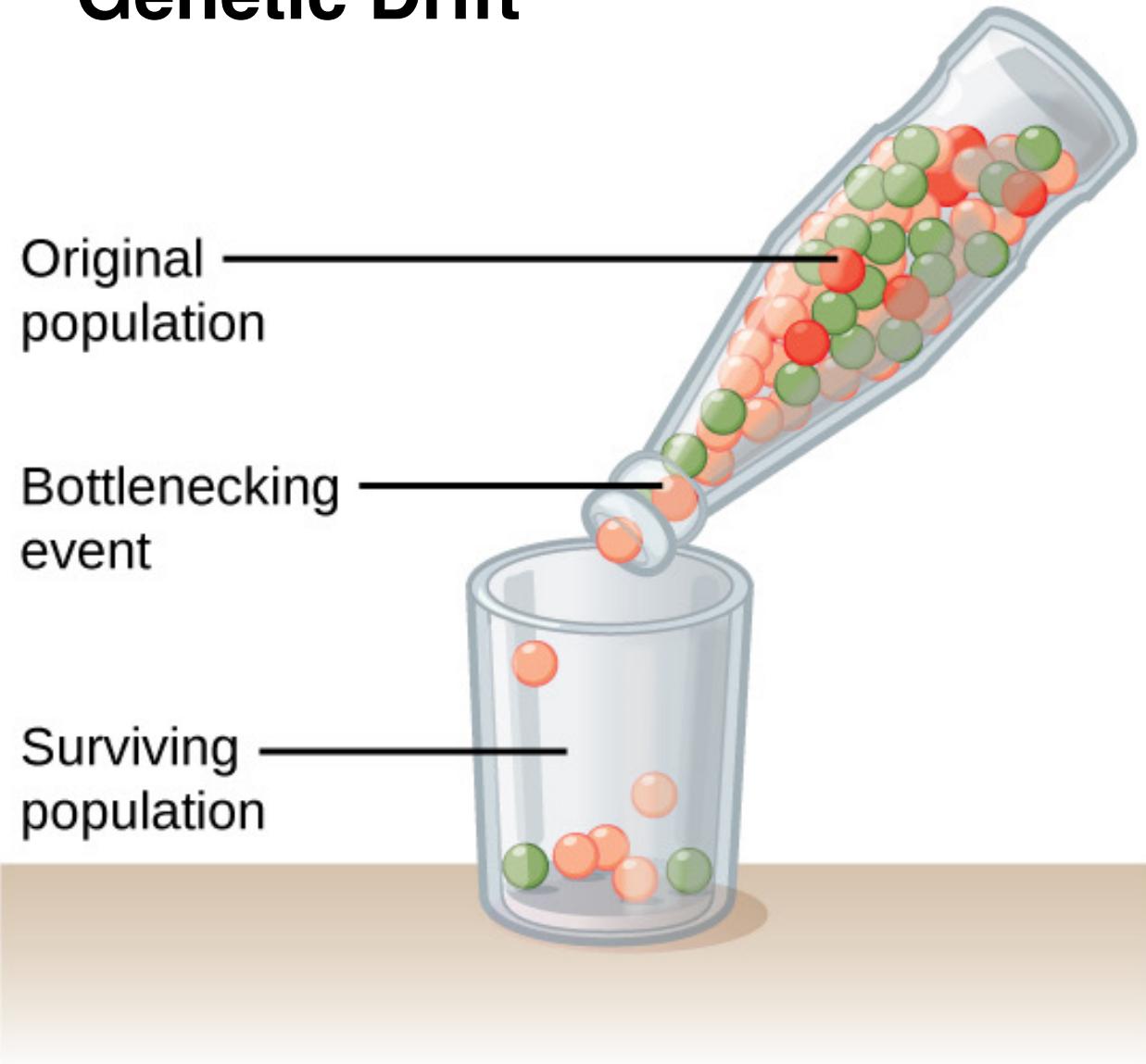
Freq A ( $p$ ) = 1

Freq C ( $q$ ) = 0

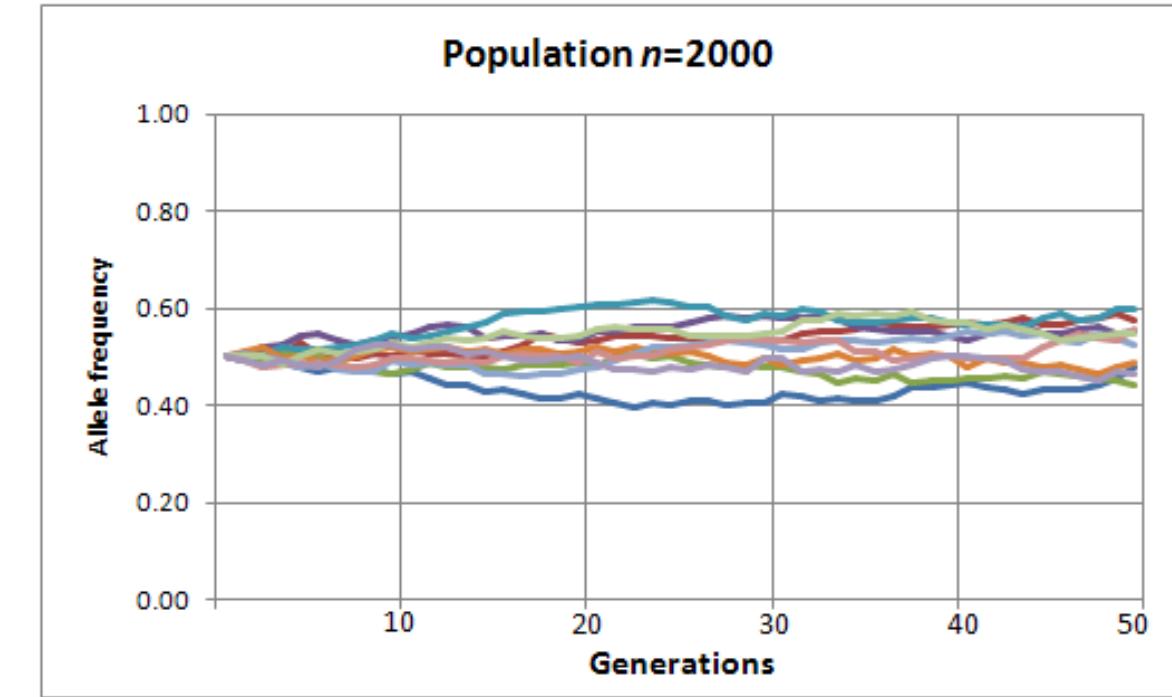
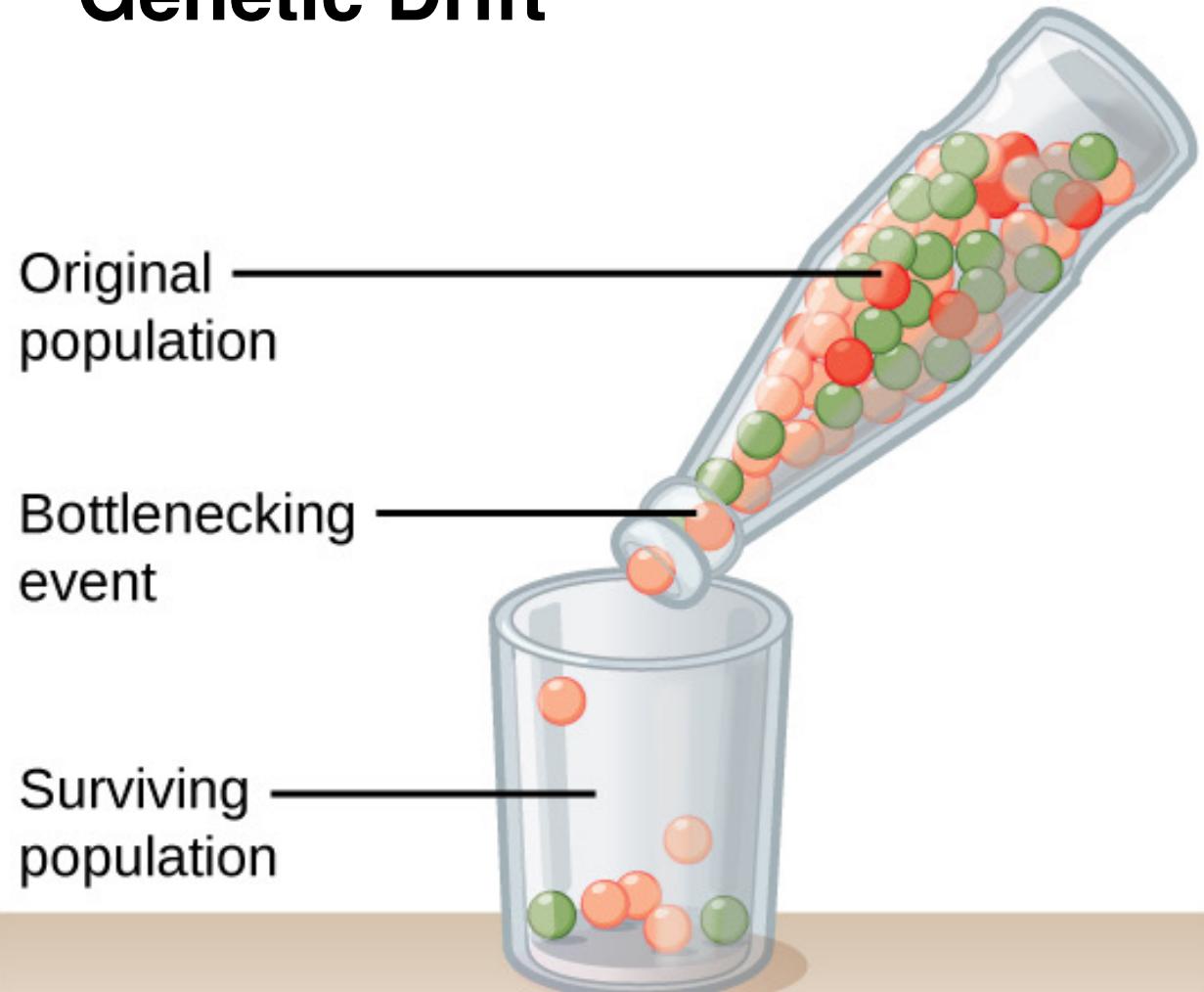


Generation 1

# Genetic Drift



# Genetic Drift

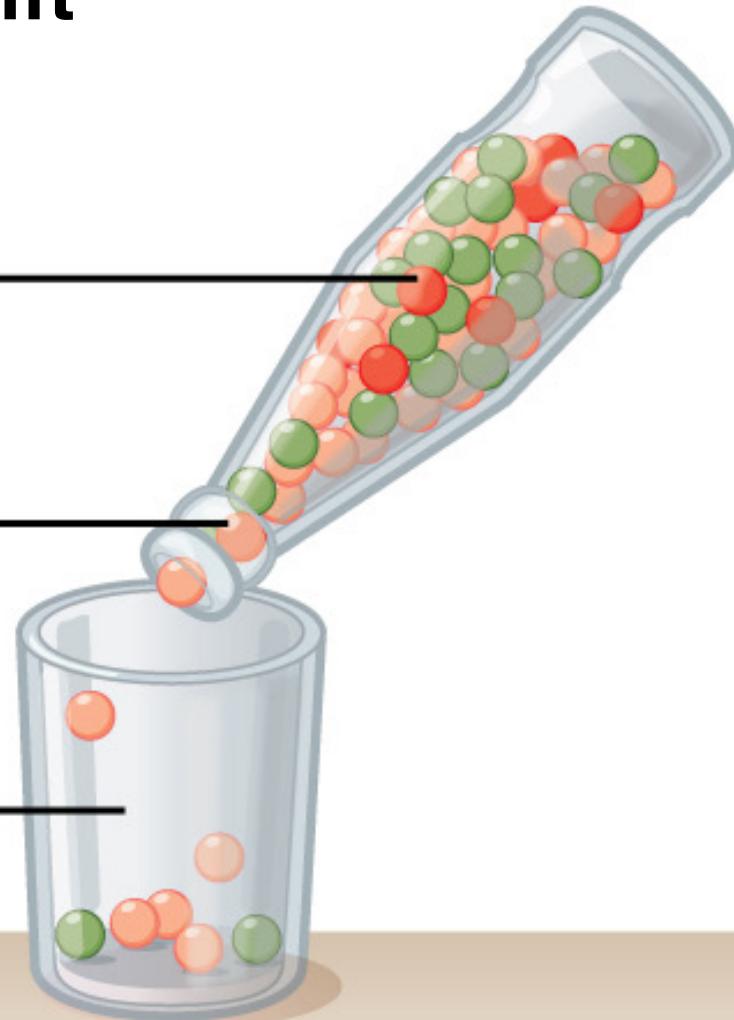


# Genetic Drift

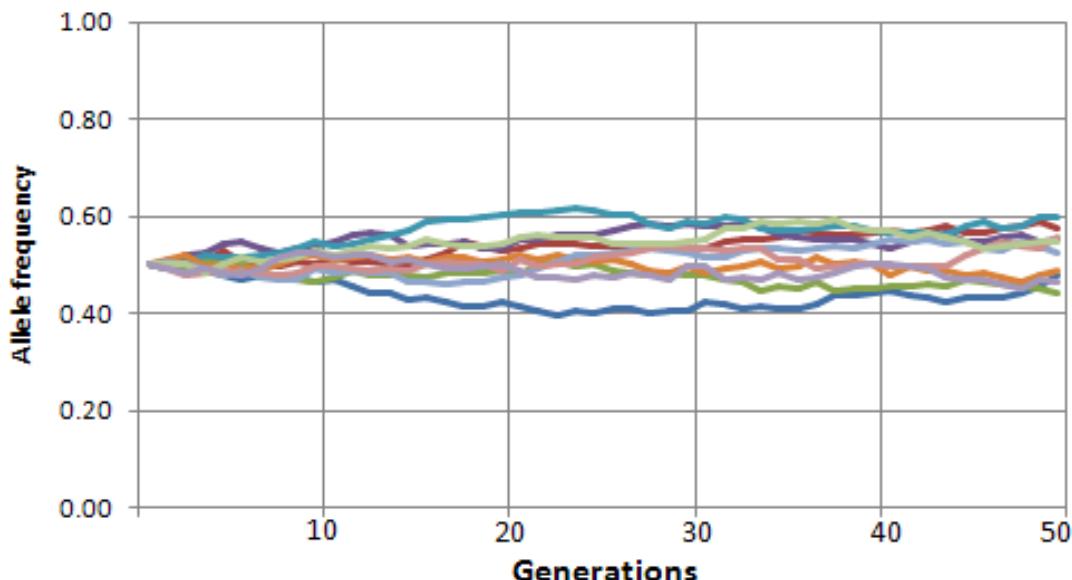
Original population

Bottlenecking event

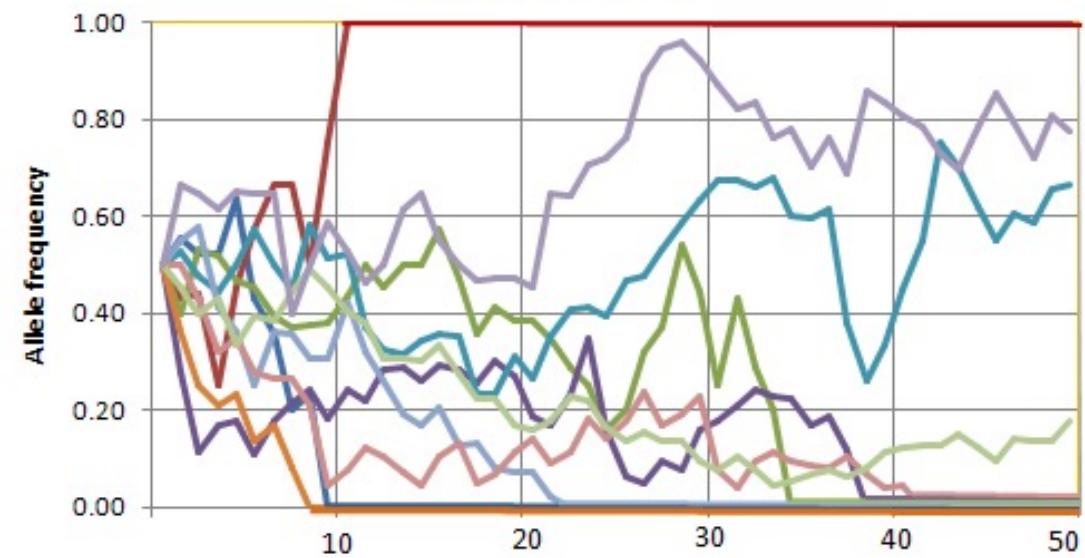
Surviving population



Population  $n=2000$



Population  $n=20$

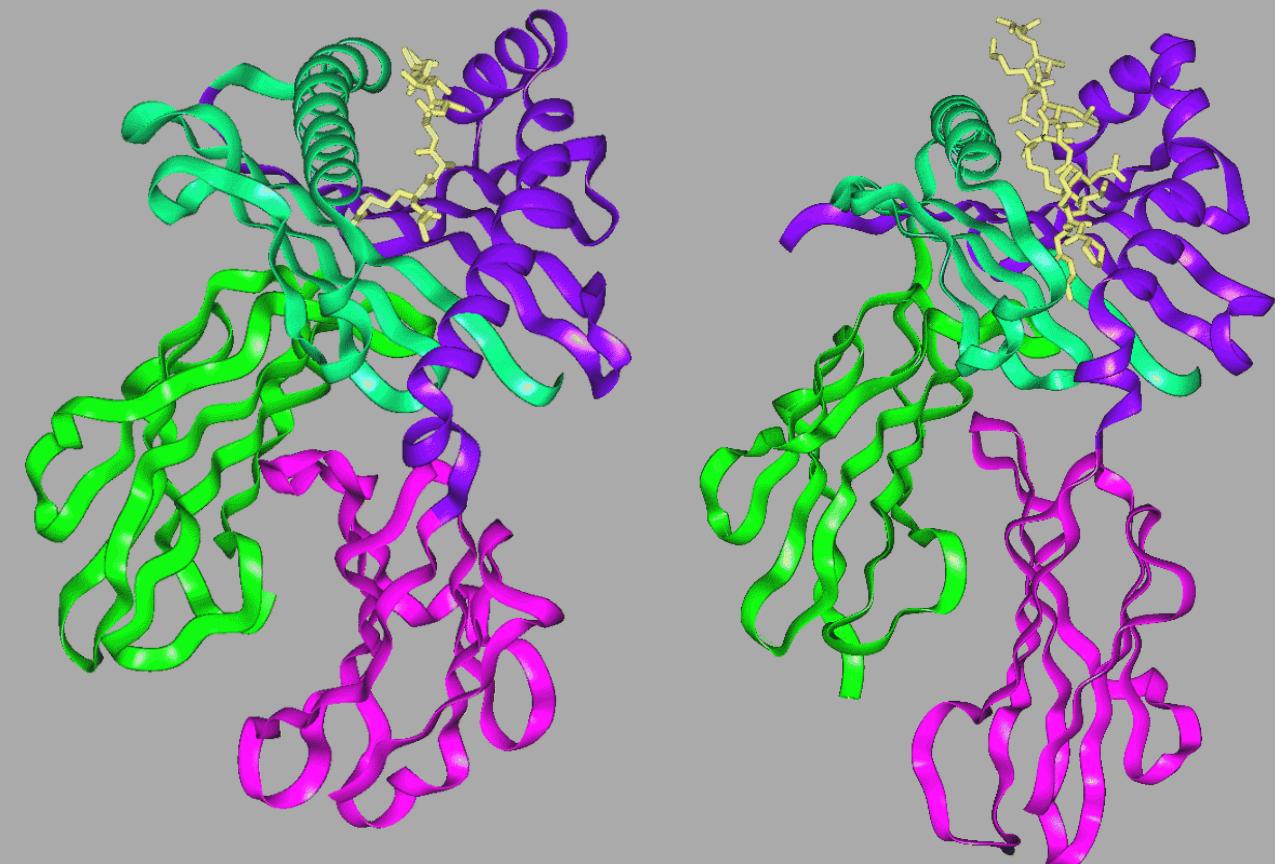




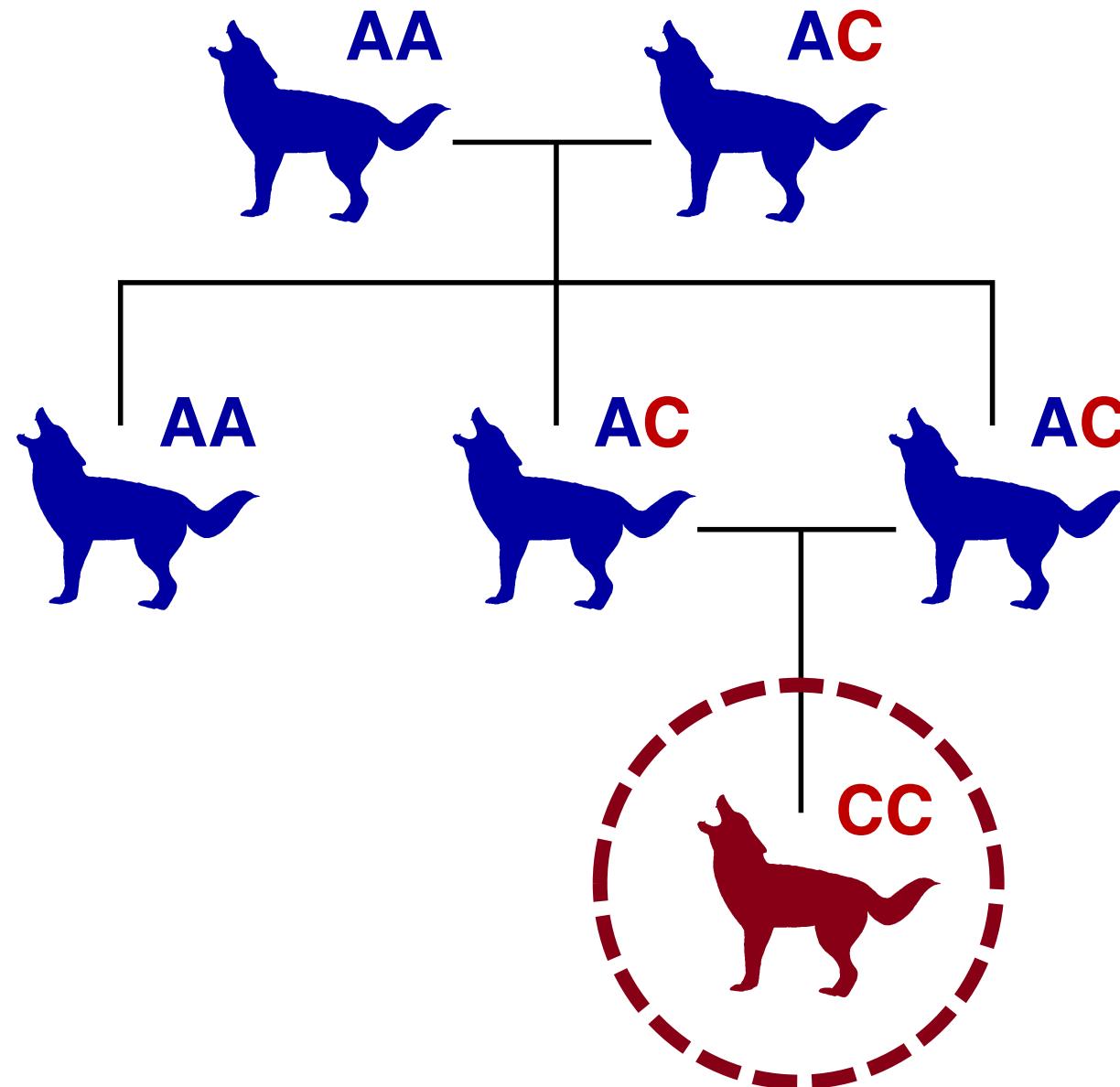
# Transmission of a fatal clonal tumor by biting occurs due to depleted MHC diversity in a threatened carnivorous marsupial

Hannah V. Siddle<sup>†</sup>, Alexandre Kreiss<sup>‡</sup>, Mark D. B. Eldridge<sup>§¶</sup>, Erin Noonan<sup>||</sup>, Candice J. Clarke<sup>††</sup>, Stephen Pyecroft<sup>||</sup>, Gregory M. Woods<sup>‡</sup>, and Katherine Belov<sup>†††</sup>

<sup>†</sup>Faculty of Veterinary Science, University of Sydney, Sydney, NSW 2006, Australia; <sup>‡</sup>Menzies Research Institute and School of Medicine, University of Tasmania, Private Bag 29, Hobart, TAS 7001, Australia; <sup>§</sup>Australian Museum, 6 College Street, Sydney, NSW 2010, Australia; <sup>¶</sup>Department of Biological Sciences, Macquarie University, North Ryde, NSW 2109, Australia; <sup>||</sup>Department of Primary Industries and Water, Animal Health Laboratory, 165 Westbury Road, Prospect, Launceston, TAS 7250, Australia



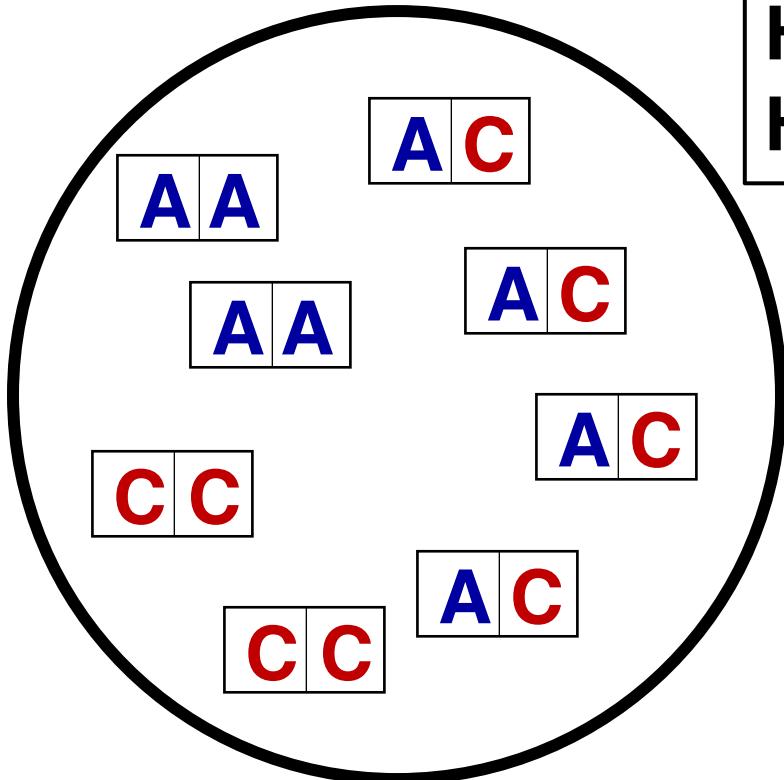
# Inbreeding



# Inbreeding

Freq A ( $p$ ) = 0.5

Freq C ( $q$ ) = 0.5



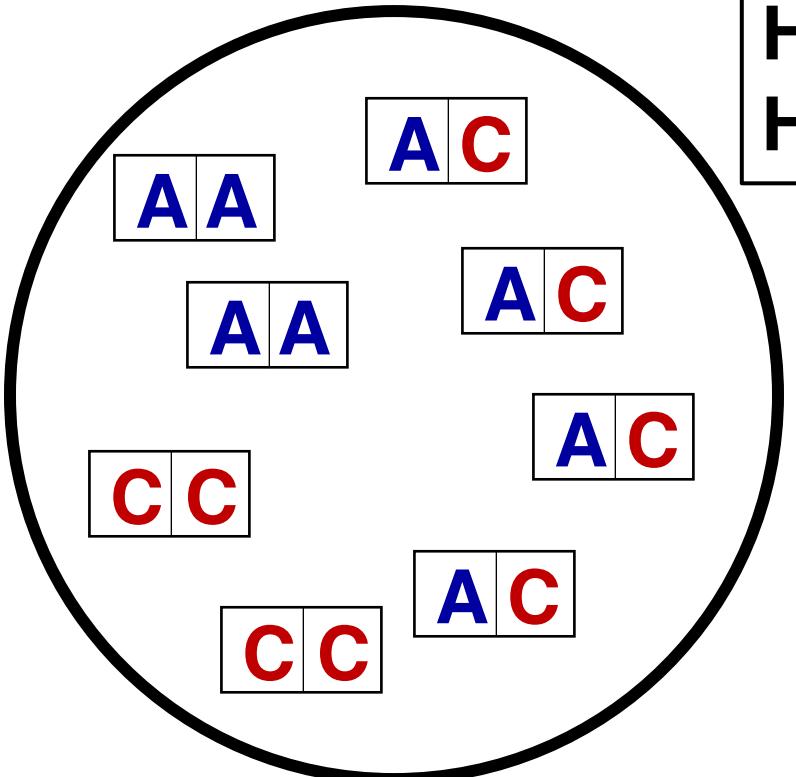
Generation 0

Homozygotes ( $p^2$ ) = 0.25  
Heterozygotes ( $2pq$ ) = 0.5  
Homozygotes ( $q^2$ ) = 0.25

# Inbreeding

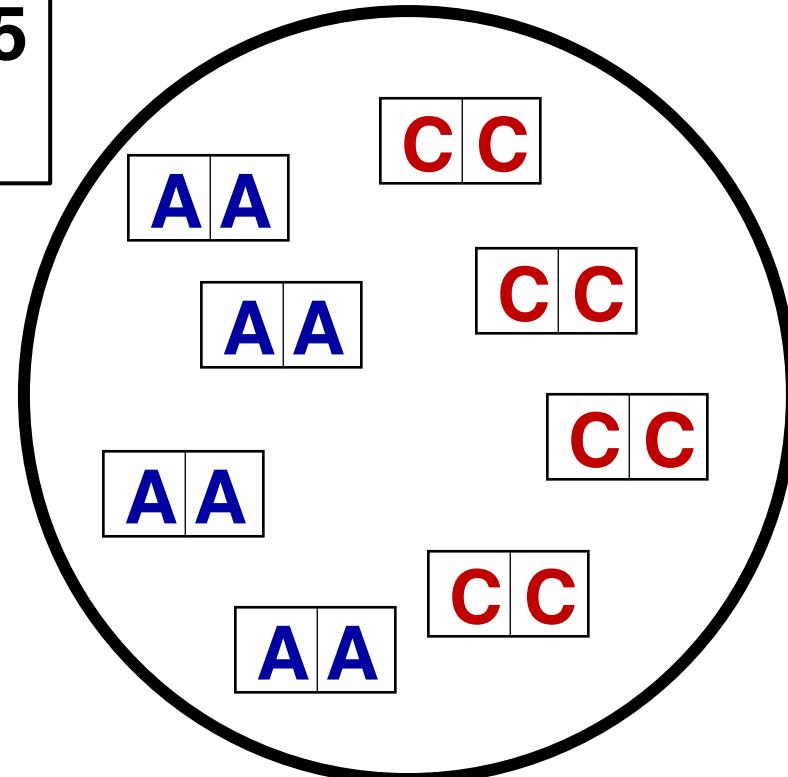
Freq A ( $p$ ) = 0.5

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Generation 0

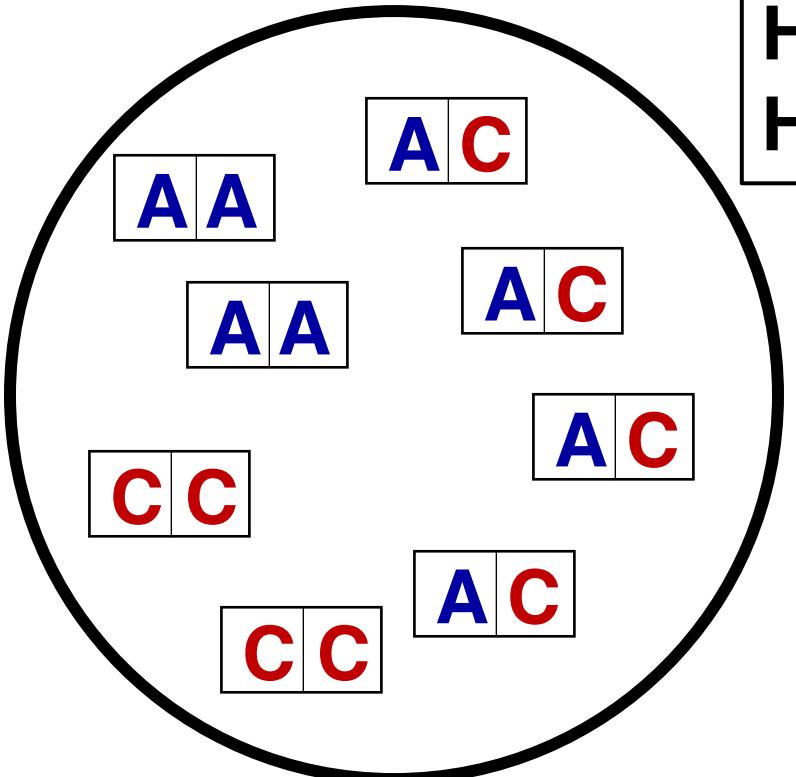
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Generation 1

# Inbreeding

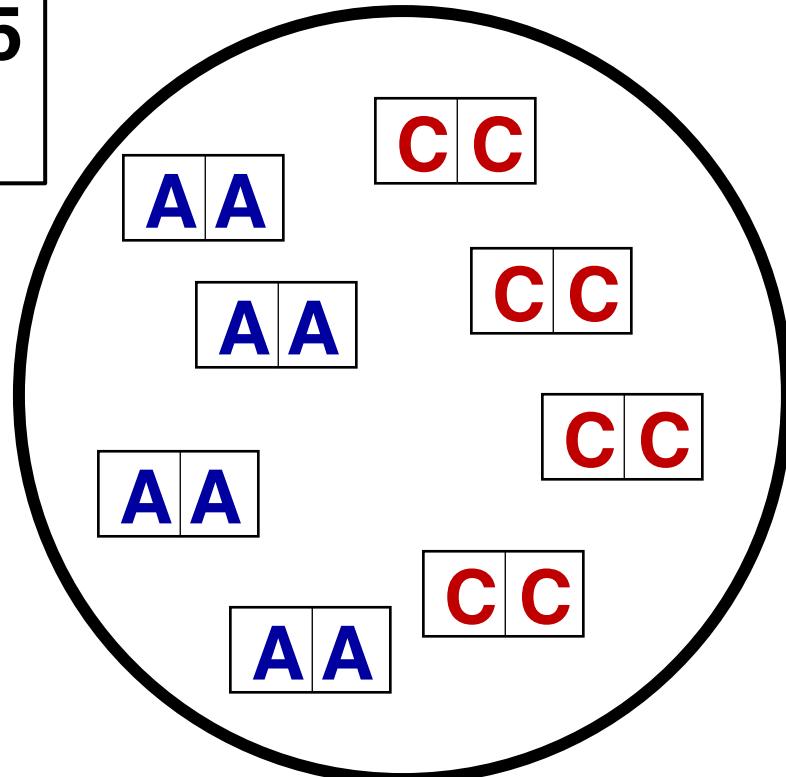
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Freq A ( $p$ ) = 0.5  
Freq C ( $q$ ) = 0.5



Generation 1

# Runs of Homozygosity (ROHs)

## Non-inbred population

Chrom 1    C G T T G G G A C C T G T T T T T  
Chrom 1    C G T G C C G A C C T A T C T T T

# Runs of Homozygosity (ROHs)

**Non-inbred population**

Chrom 1    C G T T G G G A C C T G T T T T T

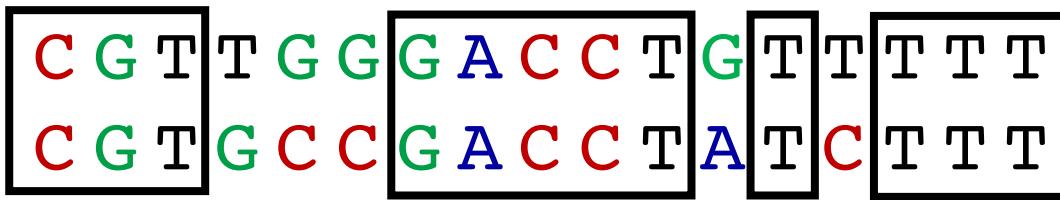
Chrom 1    C G T G C C G A C C T A T C T T T



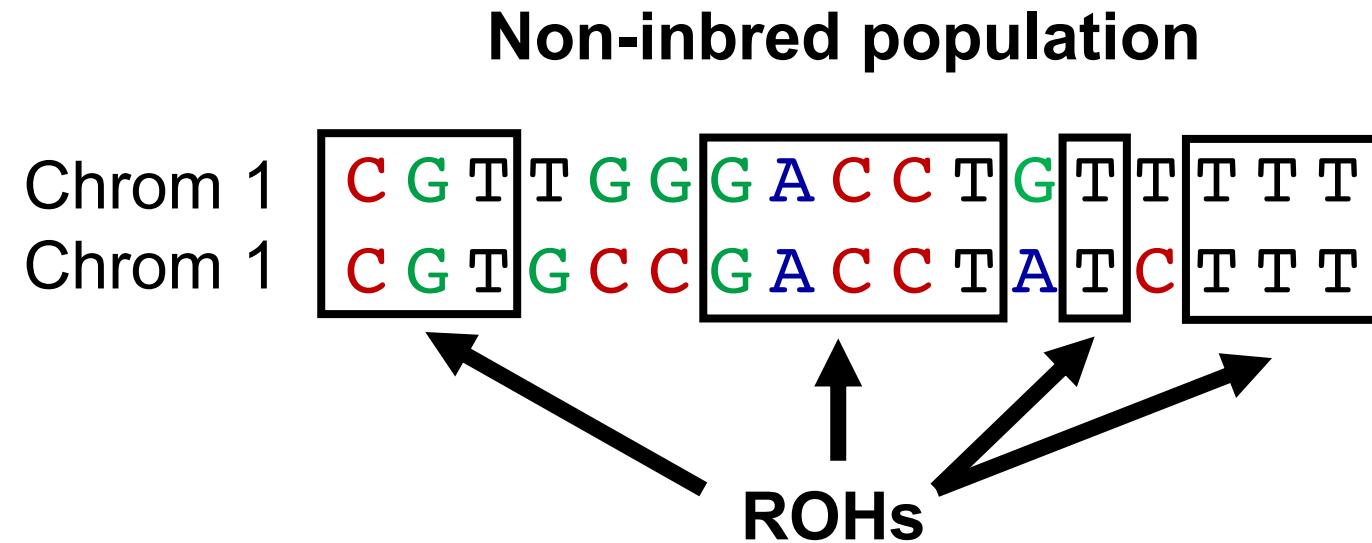
**Heterozygous genotypes**

# Runs of Homozygosity (ROHs)

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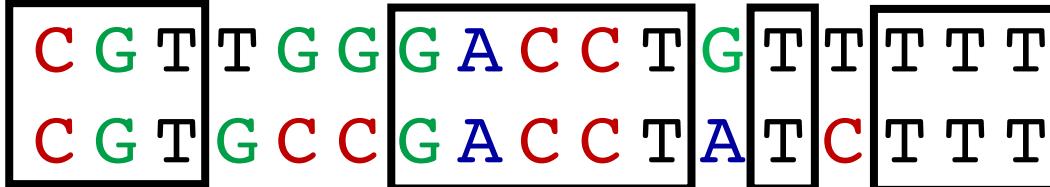
Chrom 1      
Chrom 1    

# Runs of Homozygosity (ROHs)

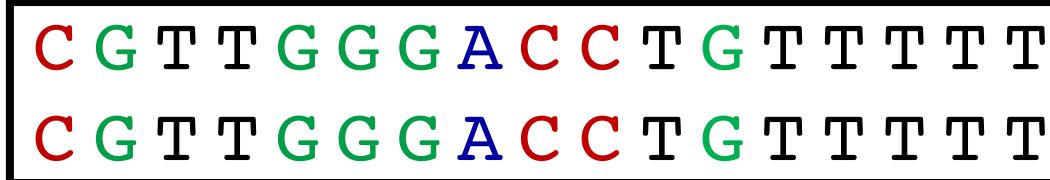


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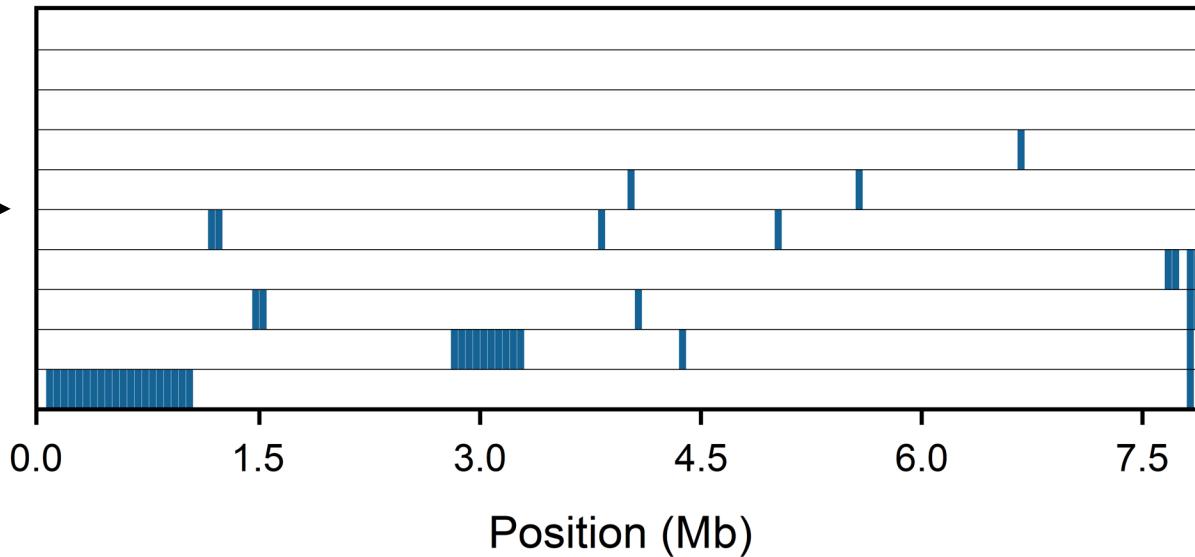
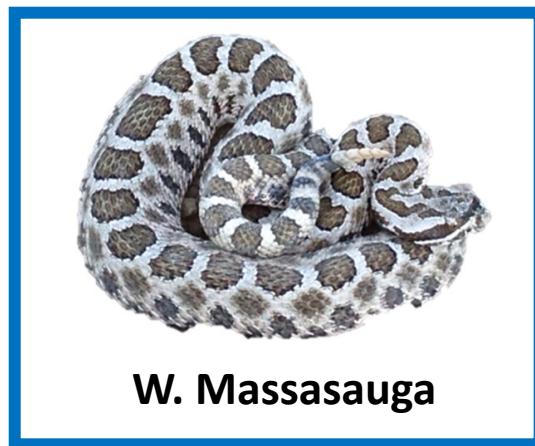
## Non-inbred population

Chrom 1      
Chrom 1    

## Inbred population

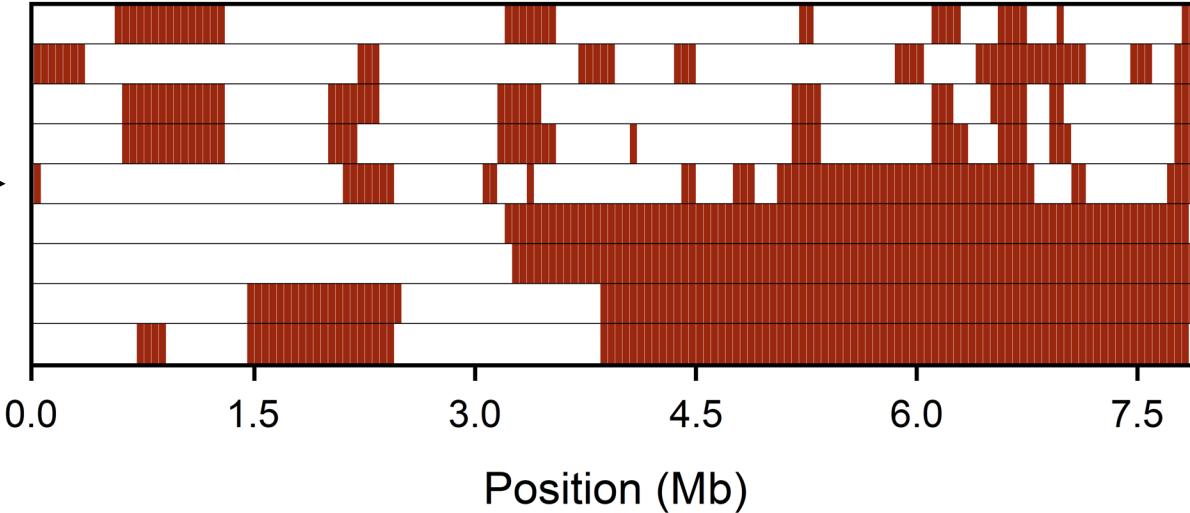
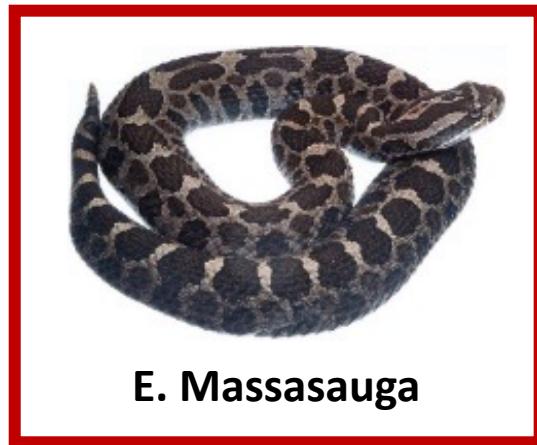
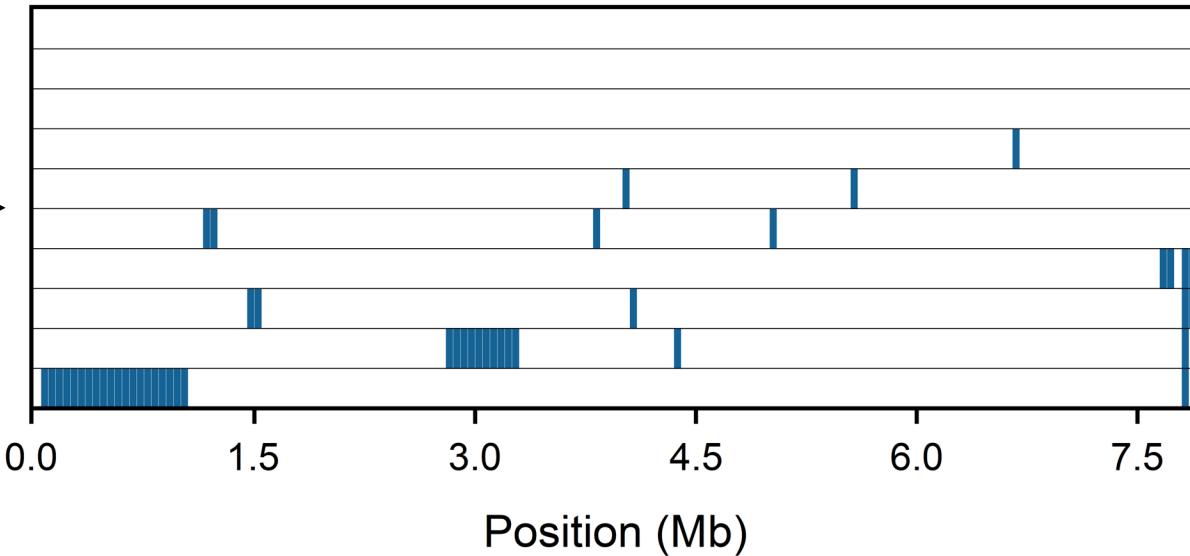
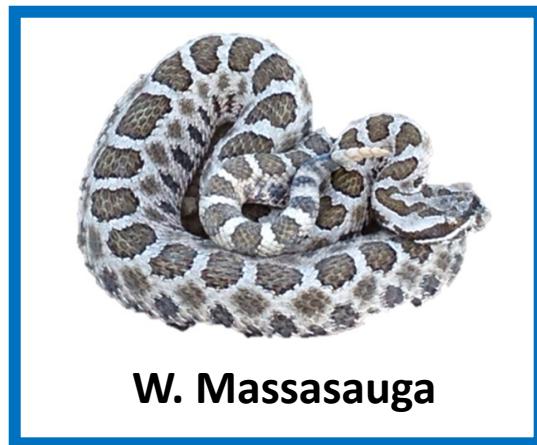
Chrom 1      
Chrom 1    

# Runs of Homozygosity (ROHs)

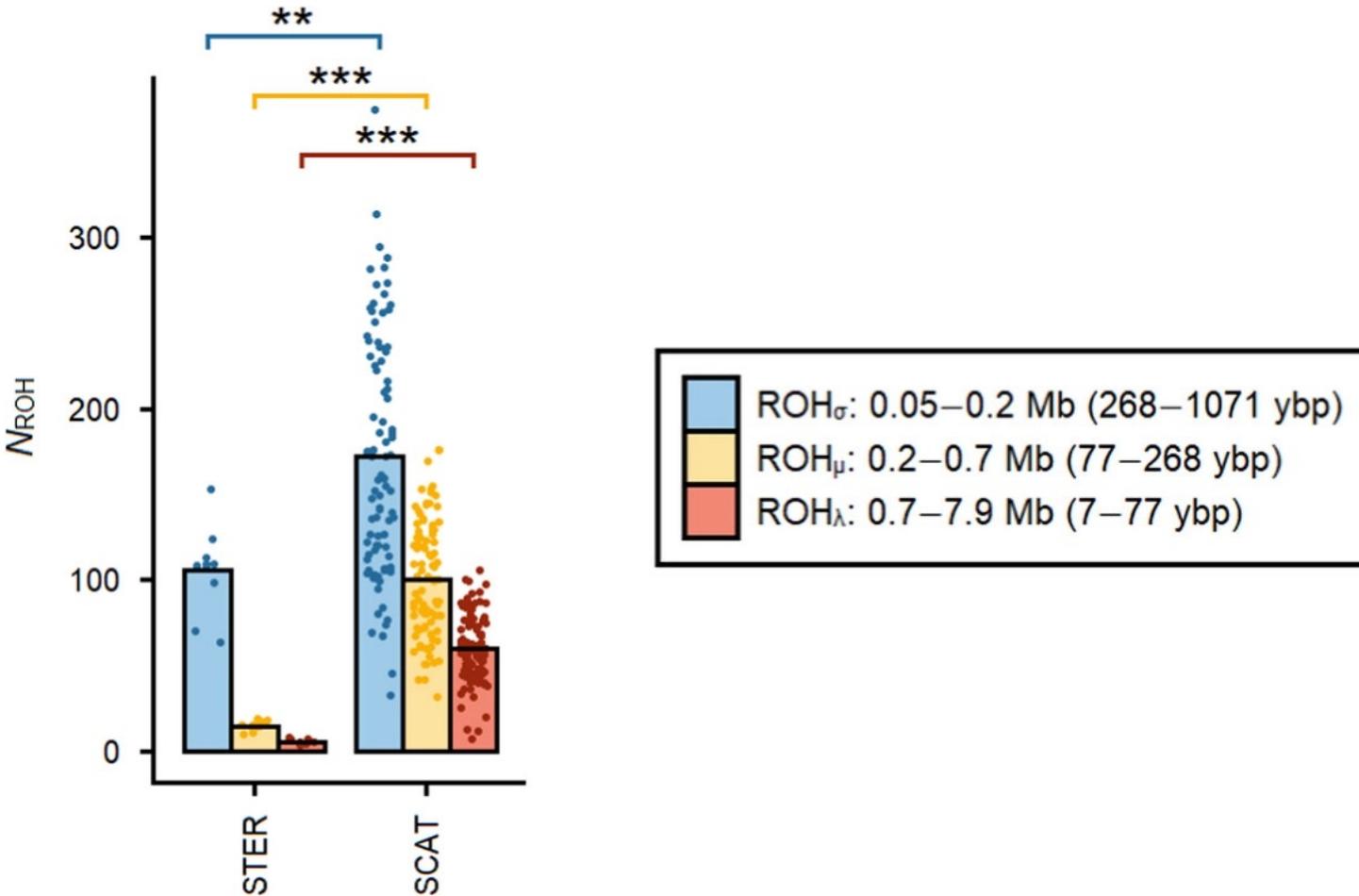


6% of the genome

# Runs of Homozygosity (ROHs)



# Runs of Homozygosity (ROHs)



# **Effective Population Size ( $N_e$ )**

“The size of an ideal population that loses heterozygosity (or becomes inbred or drifts) at the same rate as the observed population” (Frankham et al., 2010)

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# **Effective Population Size ( $N_e$ )**

“The size of an ideal population that loses heterozygosity (or becomes inbred or drifts) at the same rate as the observed population” (Frankham et al., 2010)

“The size of the breeding population” (myself and pretty much everybody else, 2023)

# $N_e/N$ Ratio



Effective population size/adult population size ratios in wildlife: a review

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E-mail: rfrankha@rna.bio.mq.edu.au*

# $N_e/N$ Ratio

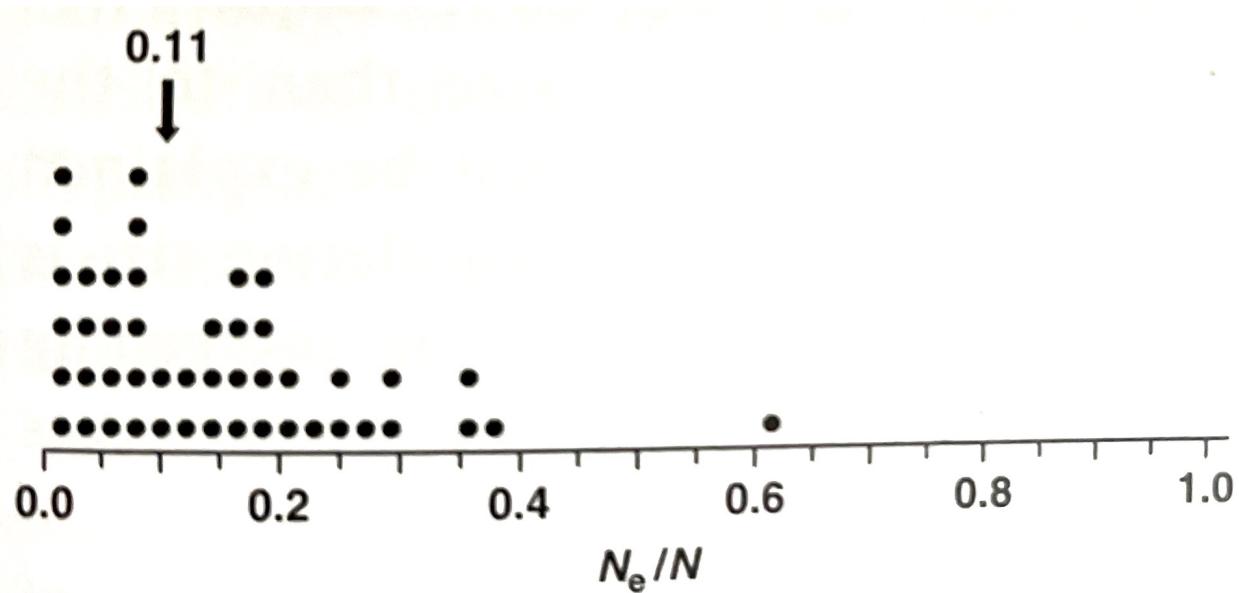


Effective population size/adult population size ratios in wildlife: a review

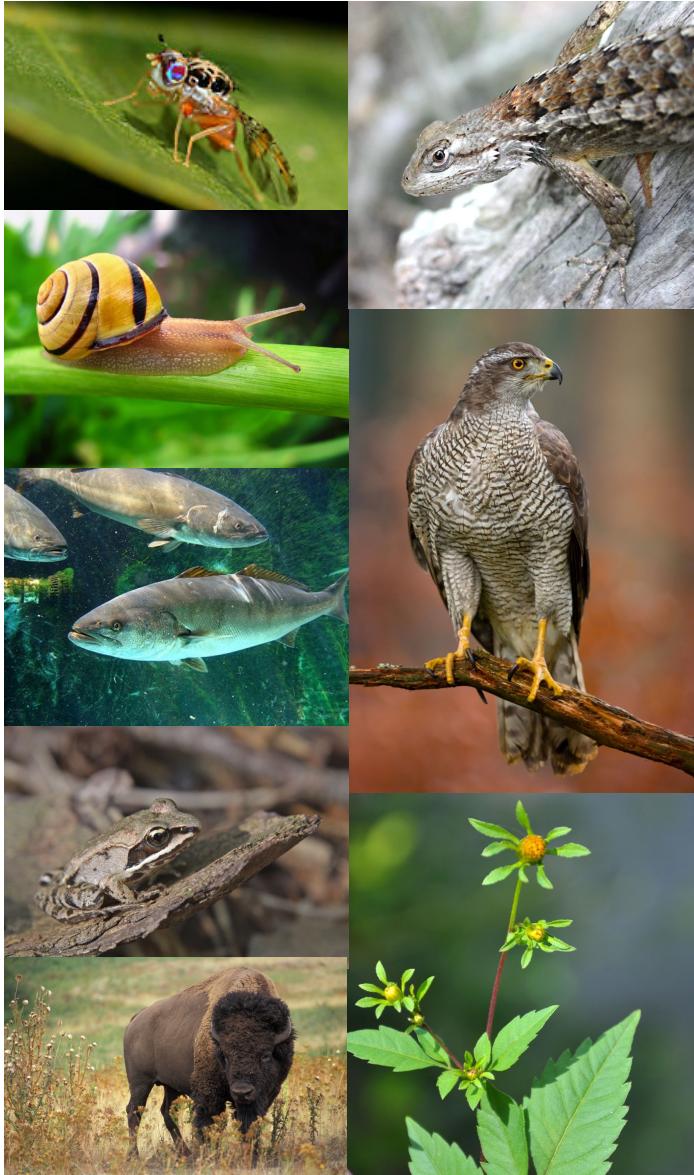
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E-mail: rfrankha@rna.bio.mq.edu.au*



# $N_e/N$ Ratio

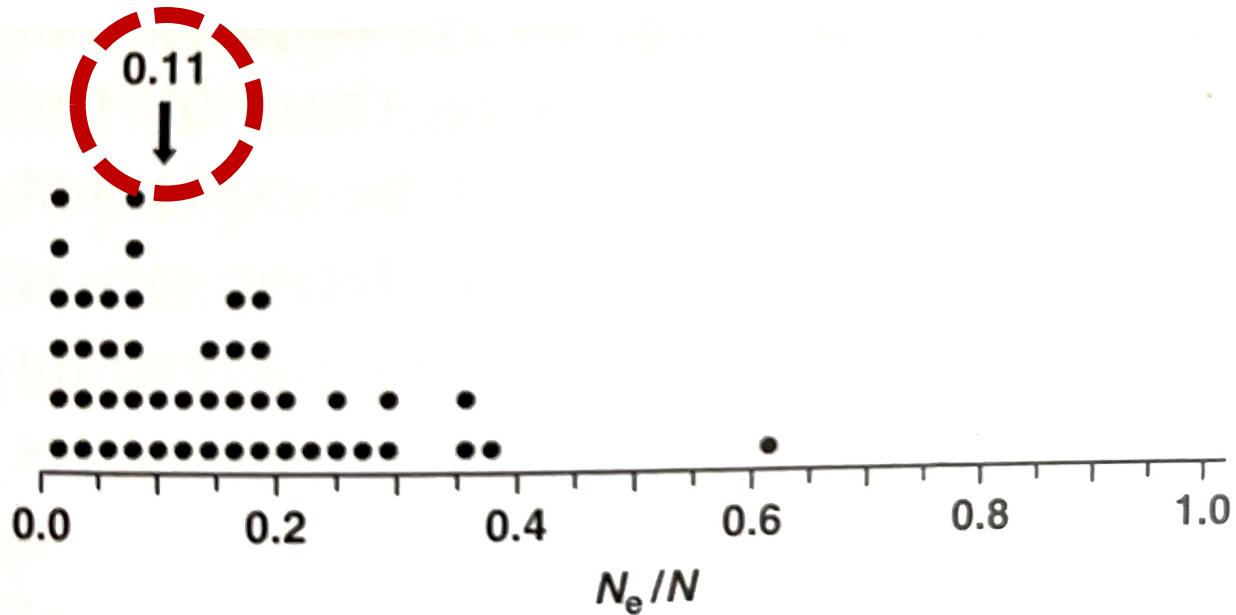


Effective population size/adult population size ratios in wildlife: a review

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E-mail: rfrankha@rna.bio.mq.edu.au*



# Measures of Genetic Variation

# Large Population

Sample_1	A A A A C A A A A A
Sample_1	A C A A A C A A A A
Sample_2	A A A C A A A A A C
Sample_2	A A A A A C A A A A
Sample_3	A A A A A A C A A A
Sample_3	A A A C A A A C A A
Sample_4	C A A A A C A A A A
Sample_4	A A A A C A A A A A
Sample_5	A A C A A A A A A A A
Sample_5	A A C A A A A A C A

# Small Population

Sample_1	A A A C A A A C A A
Sample_1	A A A C A A A C A A
Sample_2	A A A C A A A C A A
Sample_2	A A A C A A A C A A
Sample_3	A A A C A A A C A A
Sample_3	A A A C A A A A A A A
Sample_4	A A A C A A A A A A A
Sample_4	A A A C A A A A A A A
Sample_5	A A A C A A A A A A A
Sample_5	A A A C A A A A A A A

# Measures of Genetic Variation (Observed Heterozygosity)

Large Population

Sample_1	A A A A C A A A A A }	0.3
Sample_1	A C A A A C A A A A }	
Sample_2	A A A C A A A A A C }	0.3
Sample_2	A A A A A C A A A A }	
Sample_3	A A A A A A C A A A }	0.3
Sample_3	A A A C A A A C A A }	
Sample_4	C A A A A C A A A A }	0.3
Sample_4	A A A A C A A A A A }	
Sample_5	A A C A A A A A A }	0.1
Sample_5	A A C A A A A A C }	

AVG = 0.26

Small Population

Sample_1	A A A C A A A C A A }	0.0
Sample_1	A A A C A A A C A A }	
Sample_2	A A A C A A A C A A }	0.0
Sample_2	A A A C A A A C A A }	
Sample_3	A A A C A A A C A A }	0.1
Sample_3	A A A C A A A A A A }	
Sample_4	A A A C A A A A A A }	0.0
Sample_4	A A A C A A A A A A }	
Sample_5	A A A C A A A A A A }	0.0
Sample_5	A A A C A A A A A A }	

AVG = 0.02

# Measures of Genetic Variation (Segregating Sites)

Large Population

Sample_1	<b>A A A A C A A A A A A</b>
Sample_1	<b>A C A A A A C A A A A A</b>
Sample_2	<b>A A A C A A A A A A C</b>
Sample_2	<b>A A A A A A C A A A A A</b>
Sample_3	<b>A A A A A A A C A A A A</b>
Sample_3	<b>A A A C A A A A C A A A</b>
Sample_4	<b>C A A A A C A A A A A A</b>
Sample_4	<b>A A A A C A A A A A A A A</b>
Sample_5	<b>A A C A A A A A A A A A A</b>
Sample_5	<b>A A C A A A A A A A C A</b>

$$S = 10$$

Small Population

Sample_1	<b>A A A C A A A C A A A A</b>
Sample_1	<b>A A A C A A A A C A A A A</b>
Sample_2	<b>A A A C A A A A C A A A A</b>
Sample_2	<b>A A A C A A A A C A A A A</b>
Sample_3	<b>A A A C A A A A C A A A A</b>
Sample_3	<b>A A A C A A A A A A A A A A</b>
Sample_4	<b>A A A C A A A A A A A A A A</b>
Sample_4	<b>A A A C A A A A A A A A A A</b>
Sample_5	<b>A A A C A A A A A A A A A A</b>
Sample_5	<b>A A A C A A A A A A A A A A</b>

$$S = 1$$

# Measures of Genetic Variation (Nucleotide Diversity)

Large Population

Sample_1	A A A A C A A A A A A
Sample_1	A C A A A A C A A A A A
Sample_2	A A A C A A A A A A C
Sample_2	A A A A A A C A A A A A
Sample_3	A A A A A A A C A A A A
Sample_3	A A A C A A A A C A A A
Sample_4	C A A A A C A A A A A A
Sample_4	A A A A C A A A A A A A A
Sample_5	A A C A A A A A A A A A A
Sample_5	A A C A A A A A A A C A



$$\pi = \sum 2pq = 2.25$$

Small Population

Sample_1	A A A C A A A C A A A A
Sample_1	A A A C A A A A C A A A A
Sample_2	A A A C A A A A C A A A A
Sample_2	A A A C A A A A C A A A A
Sample_3	A A A C A A A A C A A A A
Sample_3	A A A C A A A A A A A A A A
Sample_4	A A A C A A A A A A A A A A
Sample_4	A A A C A A A A A A A A A A A A
Sample_5	A A A C A A A A A A A A A A A A
Sample_5	A A A C A A A A A A A A A A A A A A



$$\pi = \sum 2pq = 0.5$$

# Measures of Genetic Variation (Tajima's *D*)

$$D = \frac{\pi - \theta}{SD(\pi - \theta)}$$

# Measures of Genetic Variation (Tajima's *D*)

Nucleotide diversity

Number of segregating sites  
scaled to sample size

$$D = \frac{\pi - \theta}{SD(\pi - \theta)}$$

# Measures of Genetic Variation (Tajima's *D*)

Large Population

Sample_1	A A A A C A A A A A A
Sample_1	A C A A A A C A A A A A
Sample_2	A A A C A A A A A A C
Sample_2	A A A A A A C A A A A A
Sample_3	A A A A A A A C A A A A
Sample_3	A A A C A A A A C A A A
Sample_4	C A A A A C A A A A A A
Sample_4	A A A A C A A A A A A A A
Sample_5	A A C A A A A A A A A A A
Sample_5	A A C A A A A A A A C A



Small Population

Sample_1	A A A C A A A C A A A
Sample_1	A A A C A A A A C A A A
Sample_2	A A A C A A A A C A A A
Sample_2	A A A C A A A A C A A A
Sample_3	A A A C A A A A C A A A
Sample_3	A A A C A A A A A A A A A
Sample_4	A A A C A A A A A A A A A
Sample_4	A A A C A A A A A A A A A
Sample_5	A A A C A A A A A A A A A
Sample_5	A A A C A A A A A A A A A



# Measures of Genetic Variation (Tajima's $D$ )

# Large Population

Sample_1	A A A A C A A A A A
Sample_1	A C A A A C A A A A
Sample_2	A A A C A A A A A C
Sample_2	A A A A A C A A A A
Sample_3	A A A A A A C A A A
Sample_3	A A A C A A A C A A
Sample_4	C A A A A C A A A A
Sample_4	A A A A C A A A A A
Sample_5	A A C A A A A A A A
Sample_5	A A C A A A A A C A

$$D < 0$$

# Small Population

Sample_1	A A A C A A A C A A
Sample_1	A A A C A A A C A A
Sample_2	A A A C A A A C A A
Sample_2	A A A C A A A C A A
Sample_3	A A A C A A A C A A
Sample_3	A A A C A A A A A A A
Sample_4	A A A C A A A A A A A
Sample_4	A A A C A A A A A A A
Sample_5	A A A C A A A A A A A
Sample_5	A A A C A A A A A A A

$$D > 0$$

# Measures of Genetic Variation (Tajima's $D$ )

# Large Population

Sample_1	A A A A C A A A A A
Sample_1	A C A A A C A A A A
Sample_2	A A A C A A A A A C
Sample_2	A A A A A C A A A A
Sample_3	A A A A A A C A A A
Sample_3	A A A C A A A C A A
Sample_4	C A A A A C A A A A
Sample_4	A A A A C A A A A A A
Sample_5	A A C A A A A A A A A
Sample_5	A A C A A A A A C A

A horizontal row of ten red arrows pointing upwards, spaced evenly apart.

$$D < 0$$

# Demographic Expansion

## **Small Population**

Sample_1	A A A C A A A C A A
Sample_1	A A A C A A A C A A
Sample_2	A A A C A A A C A A
Sample_2	A A A C A A A C A A
Sample_3	A A A C A A A C A A
Sample_3	A A A C A A A A A A A
Sample_4	A A A C A A A A A A A
Sample_4	A A A C A A A A A A A
Sample_5	A A A C A A A A A A A
Sample_5	A A A C A A A A A A A

↑

$$D > 0$$

# Demographic Decline

# Final Thoughts

- In small populations drift could erode deleterious variation, while inbreeding may expose a mosaic of deleterious traits that could be purged by selection
- Is the risk worth it?



To be continued ...