

Systems of Mating:

the rules by which pairs of gametes are chosen from the local gene pool to be united in a zygote with respect to a particular locus or genetic system.

Systems of Mating:

A deme is not defined by geography but rather by a shared system of mating. Depending upon the geographical scale involved and the individuals' dispersal and mating abilities, a deme may correspond to the entire species or to a subpopulation restricted to a small local region. The Hardy-Weinberg model assumes one particular system of mating – random mating – but many other systems of mating exist.

Some Common Systems of Mating:

- Random Mating
- Inbreeding (mating between biological relatives)
- Assortative Mating (preferential mating between phenotypically similar individuals)
- Disassortative Mating (preferential mating between phenotypically dissimilar individuals)

Inbreeding: One Word, Several Meanings

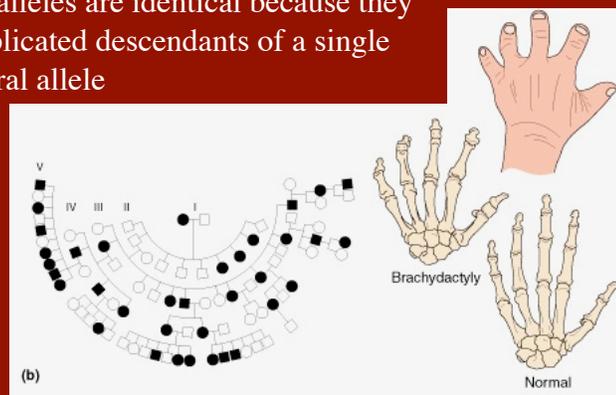
Inbreeding is mating between *biological relatives*. Two individuals are related if among the ancestors of the first individual are one or more ancestors of the second individual.

Inbreeding: One Word, Several Meanings

- Inbreeding Can Be Measured by Identity by Descent, Either for Individuals or for a Population (Because of shared common ancestors, two individuals could share genes at a locus that are identical copies of a single ancestral gene)
- Inbreeding Can Be Measured by Deviations from Random Mating in a Deme (either the tendency to preferentially mate with relatives or to preferentially avoid mating with relatives relative to random mating)

Identity by Descent

Some alleles are identical because they are replicated descendants of a single ancestral allele

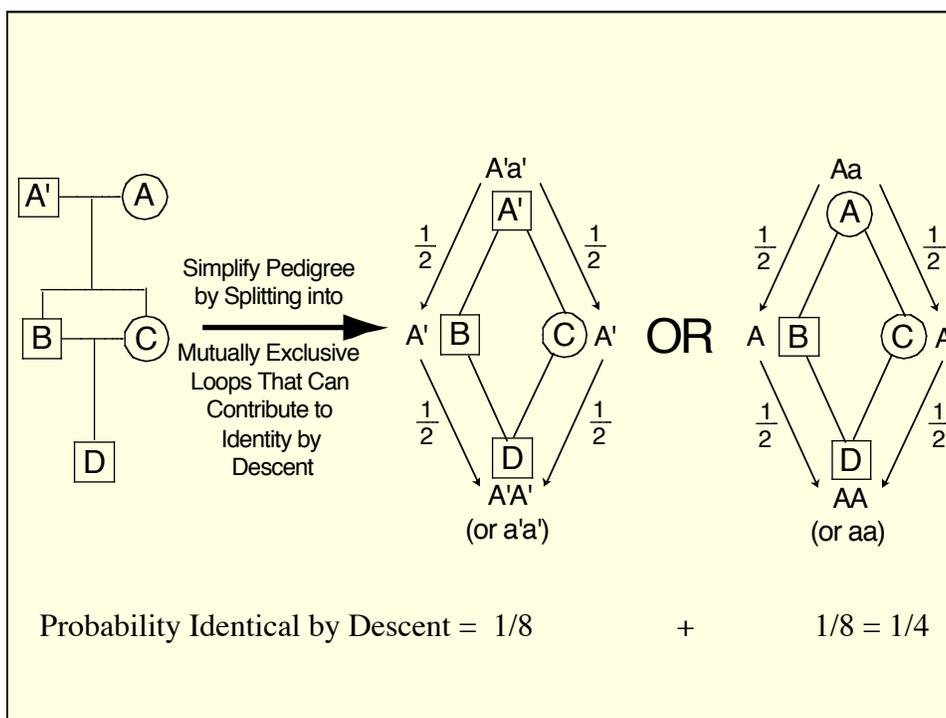
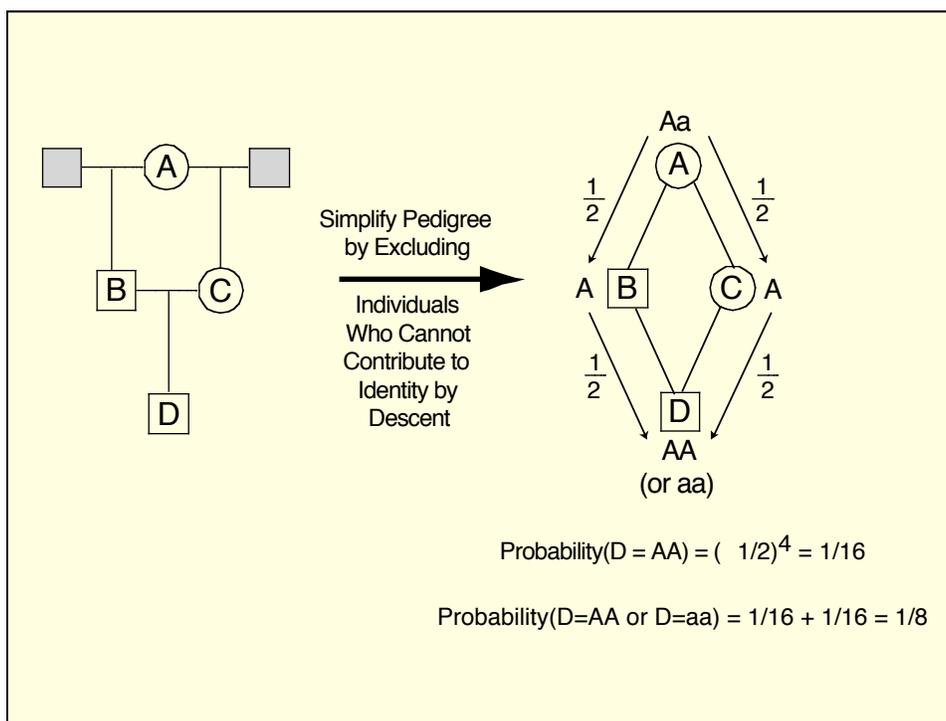


Pedigree Inbreeding, F

- Occurs when biological relatives mate
- Two individuals are related if among the ancestors of the first individual are one or more ancestors of the second individual.
- Because the father and the mother share a common ancestor, they can both pass on copies of a homologous gene that are identical by descent to their offspring.
- Such offspring are said to be homozygous due to identity by descent.

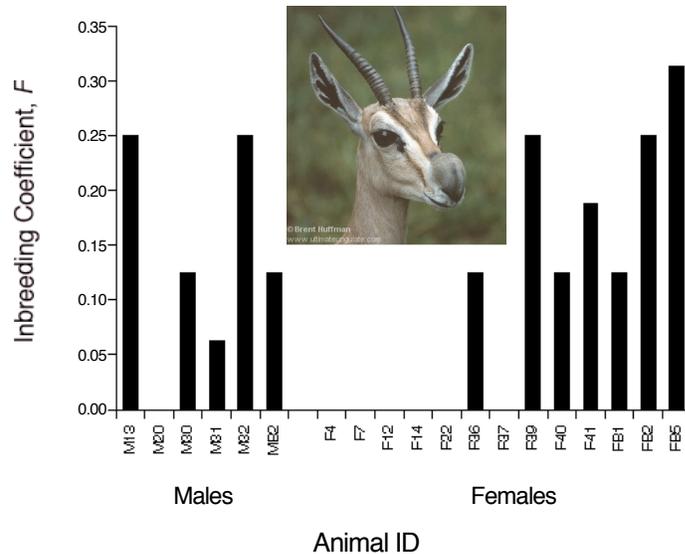
Pedigree Inbreeding Is Measured
by $F =$ Probability of
Homozygosity due to Identity by
Descent at a Randomly Chosen
Autosomal Locus

F is Called the “Inbreeding
Coefficient”



Recent work (Keller et al, Genetics 189:237-249, 2011) indicates that F due to distant ancestors not typically available in pedigree data can be estimated from runs of homozygosity in the genome (requires half a million, genome-wide SNPs & large sample sizes >1,000). Still, found most of the variation in F among individuals is due to ancestry in the last 5 generations.

F is calculated for *individuals* as a function of their pedigree (e.g., Speke's gazelle)



System of Mating refers to a deme, not individuals.

Therefore, F is *not* a measure of the system of mating.

This does not mean that pedigree inbreeding has no population or evolutionary implications.

F displays strong interactions with rare, recessive alleles and epistatic gene complexes.

Consider first a model in which a recessive allele is lethal when homozygous.

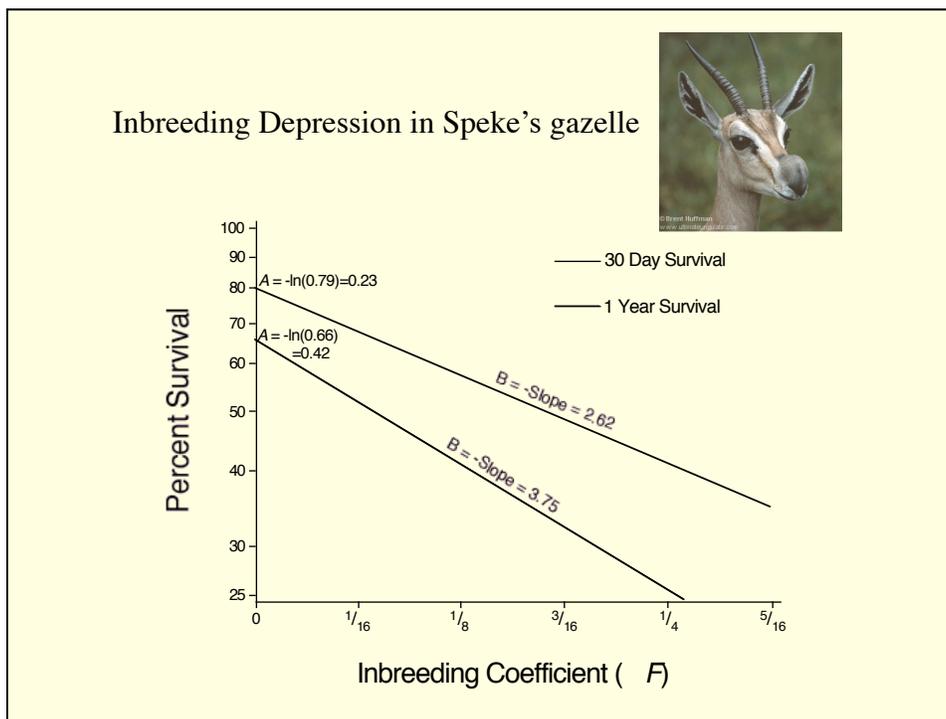
- B = the sum over all loci of the probability that a gamete drawn from the gene pool bears a recessive lethal allele at a particular locus.
- Alternatively, B = the average *number* of lethal alleles over all loci borne by a gamete in the gene pool.
- BF = the rate of occurrence of both gametes bearing lethal alleles that are identical by descent, thereby resulting in the death of the inbred individual.

Consider first a model in which a recessive allele is lethal when homozygous.

- The number of times an inbred individual will be identical-by-descent for a lethal allele will often follow a Poisson distribution.
- e^{-BF} = the probability that an individual has exactly 0 lethal genes that are identical-by-descent and therefore homozygous.
- $-A$ = the natural logarithm of the probability of not dying from any cause other than being homozygous for a lethal recessive allele that is identical-by-descent, so e^{-A} = the probability of not dying from something else.
- $e^{-BF}e^{-A} = e^{-(A+BF)}$ = probability of an individual with F being alive.
- $\ln(\text{Probability of an individual with } F \text{ being alive}) = -A - BF$

Consider first a model in which a recessive allele is lethal when homozygous.

- $\ln(\text{Probability of an individual with } F \text{ being alive}) = -A - BF$
- Because $BF > 0$, the above equation describes **inbreeding depression**, *the reduction of a beneficial trait (such as viability or birth weight) with increasing levels of pedigree inbreeding*.
- To detect and describe inbreeding depression, pool together all the animals in a **population** with the same F to estimate the probability of being alive, and then regress the $\ln(\text{prob. of being alive})$ vs. F .



F displays strong interactions with rare, recessive alleles and epistatic gene complexes.

Example of epistasis: **synthetic lethals**.

- Knock-out (complete loss of function) mutations were induced for virtually all of the 6200 genes in the yeast (*Saccharomyces cerevisiae*) genome (Tong et al. 2001. *Sci.* 294:2364-2368).
- >80% of these knock-out mutations were not lethal when made homozygous through identity by descent and classified “nonessential”
- Extensive lethality emerged when yeast strains were bred that bore homozygous pairs of mutants from this “nonessential” class.
- Therefore, B = the number of “lethal equivalents” rather than the number of actual lethal alleles.

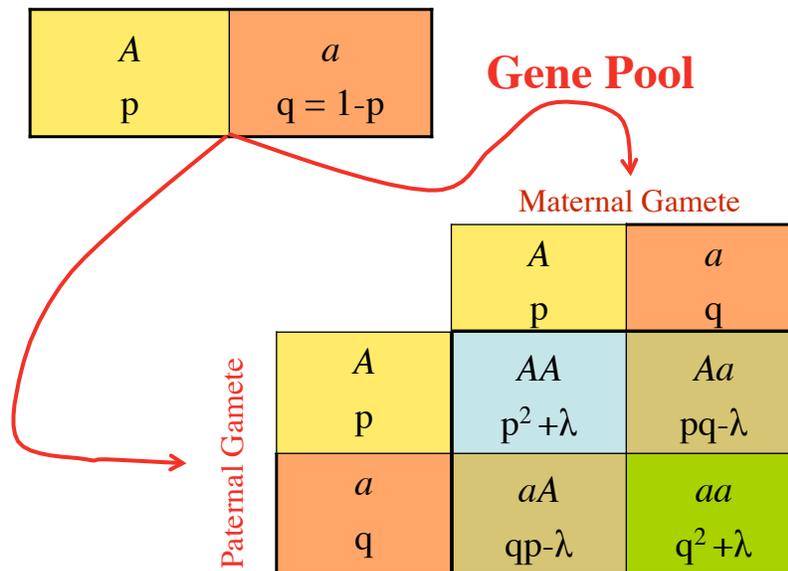
F displays strong interactions with rare, recessive alleles and epistatic gene complexes.

- $2B$ = the number of lethal equivalents in heterozygous condition that a living animal is expected to bear.
- For Speke's gazelles, the average number of lethal equivalents for one-year survivorship borne by the founding animals of this herd is therefore 7.5 lethal equivalents per animal.
- Humans from the United States and Europe yield values of $2B$ between 5-8.
- Therefore, even small amounts of pedigree inbreeding in a population may increase the incidence of some types of genetic disease by orders of magnitude in the pedigree-inbred subset of the population (e.g., 0.05% of matings in the US are between cousins, but 18-24% of albinos in the US come from cousin matings vs. an overall incidence of 0.006%).

System of Mating Inbreeding, f

- F is calculated for individuals from pedigree data.
- Demes are defined by a shared system of mating, but this is a *population* level concept.
- Therefore, we need another definition of inbreeding at the level of a deme to describe the population incidence of matings between relatives.

Inbreeding as a Deviation from Random Mating



Genotype Frequencies that Deviate From Random Mating due to λ

AA	Aa	aa
$p^2 + \lambda$	$2pq - 2\lambda$	$q^2 + \lambda$

Define $f = \lambda / (pq)$

AA	Aa	aa
$p^2 + pqf$	$2pq(1-f)$	$q^2 + pqf$

Can Estimate $f = 1 - \text{Freq}(Aa) / (2pq)$

f = panmictic index, but usually called the “inbreeding coefficient”

- Measures the rules by which gametes unite at the level of the deme
- Is a measure of system of mating
- Random mating is a special case where $f=0$
- Inbreeding is a special case where $f > 0$
- Avoidance of inbreeding is a special case where $f < 0$
- f can be shown to be the correlation between uniting gametes in the deme

Let x be a random variable that indicates the allele borne by a male gamete such that $x=1$ if the male gamete bears an A allele, and $x=0$ if the male gamete bears an a allele. Similarly, let y be a random variable that indicates the allele borne by a female gamete such that $y=1$ if the female gamete bears an A allele, and $y=0$ if the female gamete bears an a allele.

$$\text{Mean}(x) = \mu_x = 1 \times p + 0 \times q = p$$

$$\text{Mean}(y) = \mu_y = 1 \times p + 0 \times q = p$$

$$\text{Variance}(x) = \sigma_x^2 = (1 - \mu_x)^2 \times p + (0 - \mu_x)^2 \times q = (1 - p)^2 p + (-p)^2 q = pq$$

$$\text{Variance}(y) = \sigma_y^2 = pq$$

$$\begin{aligned} \text{Covariance}(x,y) &= (1 - \mu_x)(1 - \mu_y)(p^2 + \lambda) + (1 - \mu_x)(0 - \mu_y)(2pq - 2\lambda) + (0 - \mu_x)(0 - \mu_y)(q^2 + \lambda) \\ &= q^2(p^2 + \lambda) - pq(2pq - 2\lambda) + p^2(q^2 + \lambda) \\ &= \lambda(q^2 + 2pq + p^2) \\ &= \lambda \end{aligned}$$

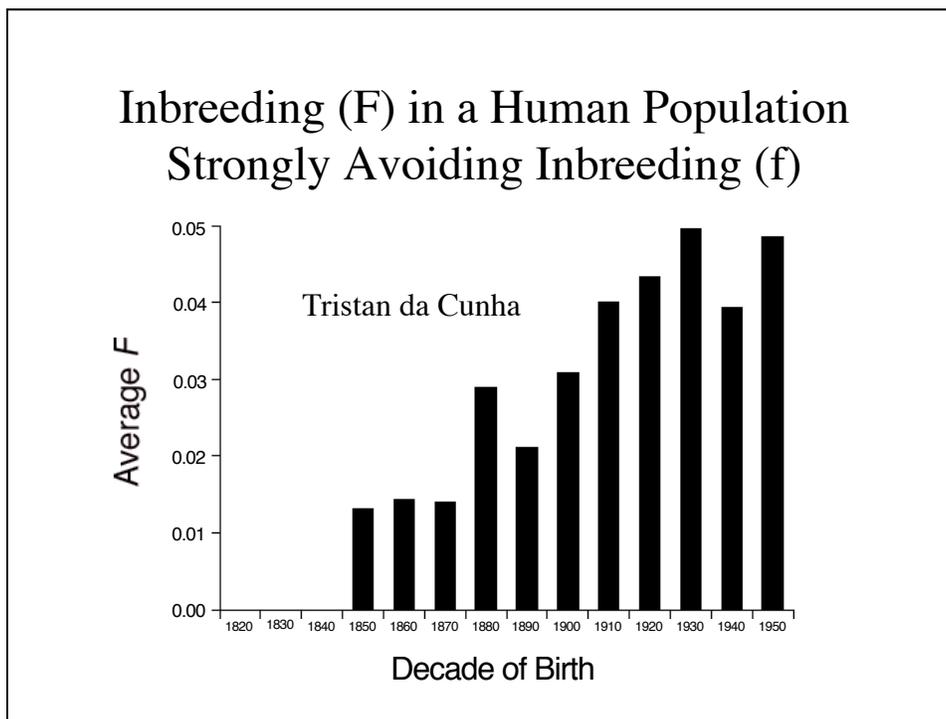
$$\rho_{x,y} = \frac{\text{Covariance}(x,y)}{\sqrt{\sigma_x^2 \sigma_y^2}} = \frac{\lambda}{pq}$$

F vs f Inbreeding Coefficient

- F measures identity by descent for an *individual*; f measures deviations from Hardy-Weinberg for a *deme*
- F is calculated from pedigree data; f is calculated from genotype frequency data
- F is a probability ($0 \leq F \leq 1$), f is a correlation ($-1 \leq f \leq 1$)

Example, 1982 Captive Herd of Speke's Gazelle

- All animals in 1982 had $F > 0$, and the average $F = 0.149$
- Therefore, this herd of Speke's Gazelle is One of the Most Highly Inbred Mammalian Populations Know.
- A genetic survey in 1982 yielded $f = -0.3$
- Therefore, this herd of Speke's Gazelle is a Mammalian Populations That Strongly Avoids Inbreeding.
- CONTRADICTION?



Impact of f

- Can greatly affect genotype frequencies, particularly that of homozygotes for rare alleles: e.g., let $q = .001$, then $q^2 = 0.000001$
Now let $f = 0.01$, then $q^2 + pqf = 0.000011$
- f is NOT an evolutionary force by itself:

$$\begin{aligned}
 p' &= (1)(p^2 + pqf) + (.5)[2pq(1-f)] \\
 &= p^2 + pq + pqf - pqf \\
 &= p(p+q) = p
 \end{aligned}$$

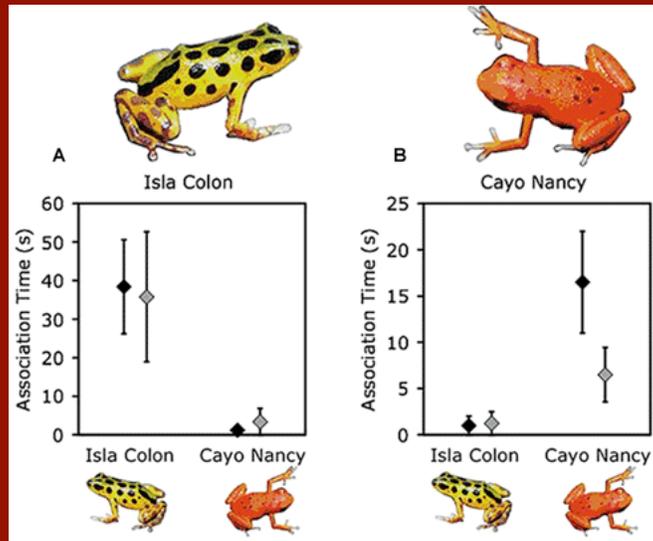
A contrast between F , the pedigree inbreeding coefficient, and f , the system-of-mating inbreeding coefficient

Property	F	f
Data Used	Pedigree Data	Genotype Frequency Data
Type of Measure	Probability	Correlation Coefficient
Range	$0 \leq F \leq 1$	$-1 \leq f \leq 1$
Level	Individual	Deme
Biological Meaning	Probability of Identity-by-Descent	System of Mating or HW Deviation

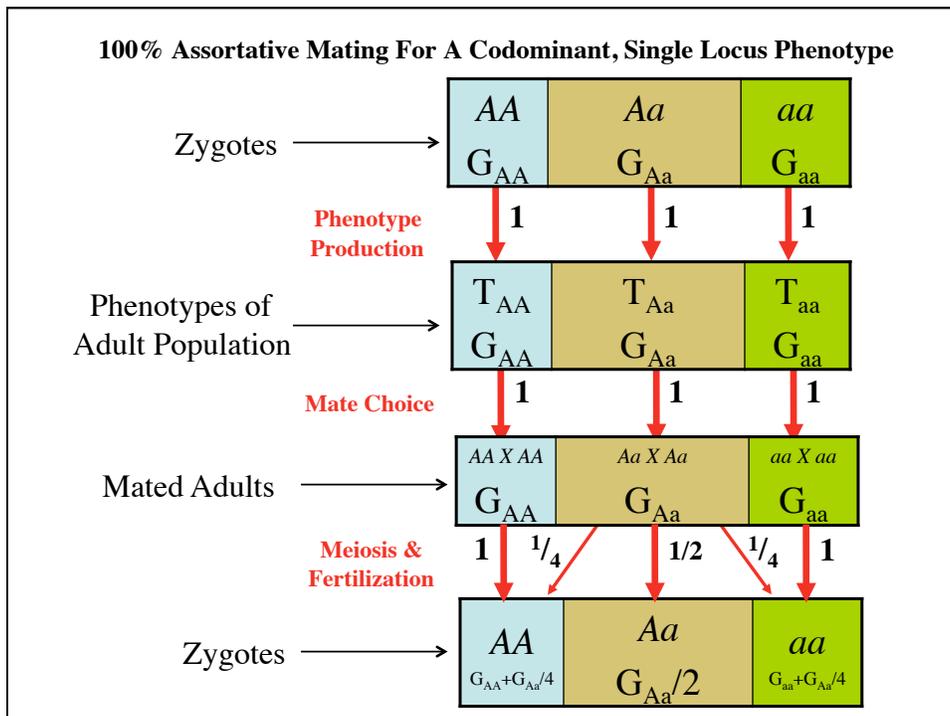
Assortative Mating

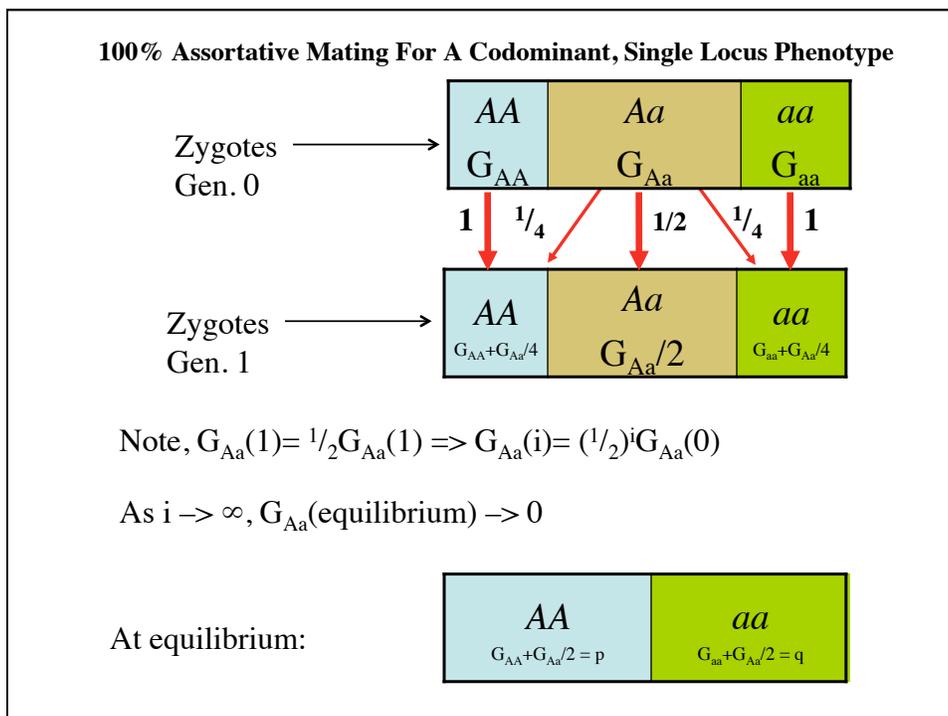
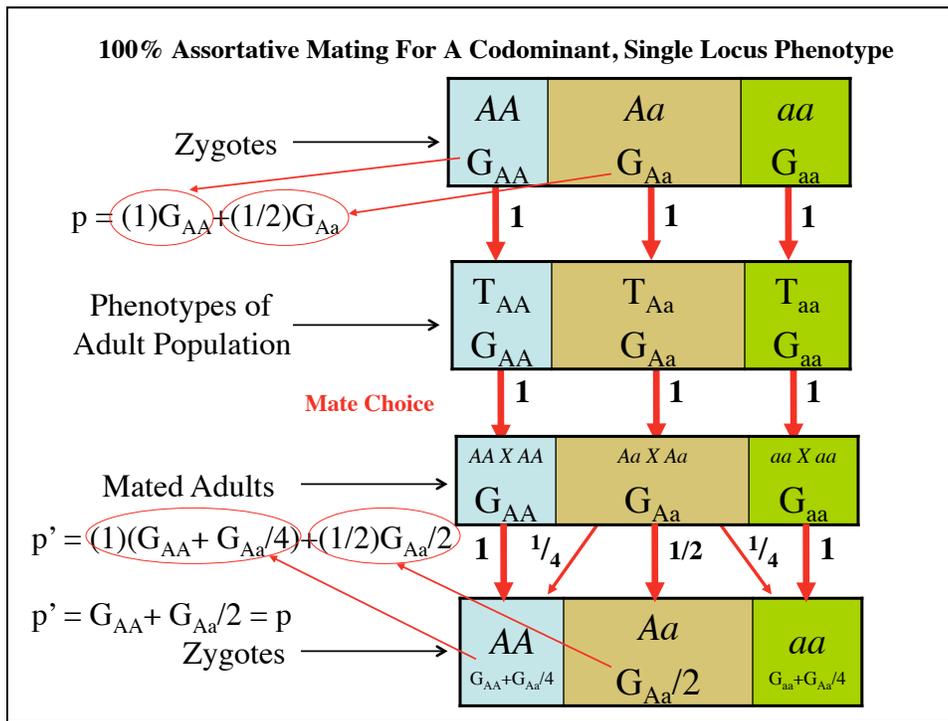
occurs when individuals with similar phenotypes are more likely to mate than expected under random pairing in the population

Assortative Mating



Reynolds, R. Graham & Fitzpatrick, Benjamin M. *Evolution* 61 (9), 2253-2259.





Profound, Early Onset Deafness

- Assortative Mating Rates Vary From 80% to 94% in USA and Europe.
- About half of the cases are due to accidents and disease
- The other half of the cases are due to homozygosity for a recessive allele at any one of 35 loci.
- Half of the genetic cases are due to homozygosity for a recessive allele at the *GJB2* locus that encodes the gap-junction protein connexin-26, with $q \approx 0.01$ in European and USA populations.

GJB2 locus, Alleles *A* and *a*

- Frequency of *a* is about 0.01 in U.S.A. & Europe
- Under random mating expect an *aa* genotype frequency of $(0.01)^2 = 0.0001$ who will be deaf
- Actual incidence of deafness due to *aa* is 0.0003 to 0.0005 (as if $f=0.02$ to 0.04)
- 3 to 5 times more children are deaf due to this gene because of assortative mating.

GJB2 locus, Alleles *A* and *a*

- Only a quarter of the people with profound early onset deafness are *aa*.
- Within matings of deaf people, therefore expect $(1/4)(1/4) = 1/16$ to be *aa* X *aa*.
- But 1/6 of the children of deaf couples are *aa*!
- In many of these couples, one of the parents is deaf due to homozygosity for a recessive allele at *another* locus, yet this person is also *Aa* at the *GJB2* locus.

GJB2 locus, Alleles *A* and *a*

- Consider a second locus with alleles *B* and *b* such that *bb* is deaf and frequency of *b* is 0.0001.
- Under random mating equilibrium, expected frequency of *ab* gametes is $(0.01)(0.0001) = 0.000001$
- But assortative mating implies that the rare *bb* individuals will mate 1/4 of the time with *aa* individuals, and the children of such matings can produce *ab* gametes.
- THEREFORE, ASSORTATIVE MATING CREATES LINKAGE DISEQUILIBRIUM!

2-Locus, 2-Allele 100% Assortative Mating With Additive Phenotypes											
Mating Type	Mate Phenotype	Offspring Genotypes									
		ΔB ΔB	ΔB Δb	ΔB aB	ΔB ab	Δb aB	Δb Δb	aB Δb	aB aB	aB ab	ab aB
$\frac{AB}{AB} \times \frac{AB}{AB}$	"4"	1									
$\frac{AB}{Ab} \times \frac{AB}{Ab}$	"3"	$\frac{1}{4}$	$\frac{1}{2}$				$\frac{1}{4}$				
$\frac{AB}{Ab} \times \frac{AB}{aB}$	"3"	$\frac{1}{4}$	$\frac{1}{4}$	$\frac{1}{4}$		$\frac{1}{4}$					
$\frac{AB}{aB} \times \frac{AB}{aB}$	"3"	$\frac{1}{4}$		$\frac{1}{2}$				"			
$\frac{AB}{ab} \times \frac{AB}{ab}$	"2"	$\frac{1}{4}(1-r)^2$	$\frac{1}{2}(1-r)r$	$\frac{1}{4}(1-r)r$	$\frac{1}{4}(1-r)^2$	$\frac{1}{4}r^2$	$\frac{1}{4}r^2$	$\frac{1}{4}r^2$	$\frac{1}{2}(1-r)r$	$\frac{1}{2}(1-r)r$	$\frac{1}{4}(1-r)^2$
$\frac{AB}{ab} \times \frac{Ab}{aB}$	"2"	$\frac{1}{4}(1-r)r$	$\frac{1}{4}(1-r)^2 + \frac{1}{4}r^2$	$\frac{1}{4}(1-r)r^2 + \frac{1}{4}r^2$	$\frac{1}{2}(1-r)r$	$\frac{1}{2}(1-r)r$	$\frac{1}{4}(1-r)r$	$\frac{1}{4}(1-r)^2 + \frac{1}{4}r^2$	$\frac{1}{4}(1-r)r$	$\frac{1}{4}(1-r)r^2 + \frac{1}{4}r^2$	$\frac{1}{4}(1-r)r$
$\frac{AB}{ab} \times \frac{Ab}{Ab}$	"2"		$\frac{1}{2}(1-r)$			$\frac{1}{2}r$	$\frac{1}{2}r$		$\frac{1}{2}(1-r)$		
$\frac{AB}{aB} \times \frac{aB}{aB}$	"2"			$\frac{1}{2}(1-r)$		$\frac{1}{2}r$		$\frac{1}{2}r$		$\frac{1}{2}(1-r)$	
$\frac{Ab}{aB} \times \frac{Ab}{aB}$	"2"	$\frac{1}{4}r^2$	$\frac{1}{2}(1-r)r$	$\frac{1}{2}(1-r)r$	$\frac{1}{4}r^2$	$\frac{1}{4}(1-r)^2$	$\frac{1}{4}(1-r)^2$	$\frac{1}{4}(1-r)^2$	$\frac{1}{2}(1-r)r$	$\frac{1}{2}(1-r)r$	$\frac{1}{4}r^2$
$\frac{Ab}{aB} \times \frac{Ab}{Ab}$	"2"		$\frac{1}{2}r$			$\frac{1}{2}(1-r)$	$\frac{1}{2}(1-r)$		$\frac{1}{2}r$		
$\frac{Ab}{aB} \times \frac{aB}{aB}$	"2"			$\frac{1}{2}r$		$\frac{1}{2}(1-r)$		$\frac{1}{2}(1-r)$		$\frac{1}{2}r$	
$\frac{Ab}{aB} \times \frac{aB}{Ab}$	"2"						1				
$\frac{Ab}{aB} \times \frac{aB}{aB}$	"2"					1					
$\frac{Ab}{aB} \times \frac{aB}{aB}$	"2"							1			
$\frac{Ab}{aB} \times \frac{Ab}{aB}$	"1"						$\frac{1}{4}$		$\frac{1}{2}$		$\frac{1}{4}$
$\frac{Ab}{aB} \times \frac{Ab}{aB}$	"1"					$\frac{1}{4}$			$\frac{1}{4}$	$\frac{1}{4}$	$\frac{1}{4}$
$\frac{aB}{aB} \times \frac{aB}{aB}$	"1"							"		$\frac{1}{2}$	$\frac{1}{4}$
$\frac{aB}{aB} \times \frac{aB}{aB}$	"0"										1

Equilibrium Populations Possible Under a 2-Locus, 2-Allele 100% Assortative Mating With Additive Phenotypes

Genotypes	Initial Gene Pool		
	$p_A = p_B$	$p_A < p_B$	$p_A > p_B$
AB/AB	p_A	p_A	p_B
Ab/Ab	0	0	$p_A - p_B$
aB/aB	0	$p_B - p_A$	0
ab/ab	p_b	p_b	p_a

Note, can start with $D=0$, but all equilibrium populations have $|D'|=1$

Properties of Assortative Mating

- Increases the Frequency of Homozygotes Relative to Hardy-Weinberg For Loci Contributing to the Phenotype Or For Loci Correlated For Any Reason to the Phenotype
- Does Not Change Allele Frequencies --Therefore Is Not An Evolutionary Forces at the Single Locus Level
- Assortative Mating Creates Disequilibrium Among Loci that Contribute to the Phenotype and Is A Powerful Evolutionary Force at the Multi-Locus Level
- Multiple Equilibria Exist at the Multi-Locus Level And The Course of Evolution Is Constrained By the Initial Gene Pool: historical factors are a determinant of the course of evolution

Assortative Mating & Inbreeding

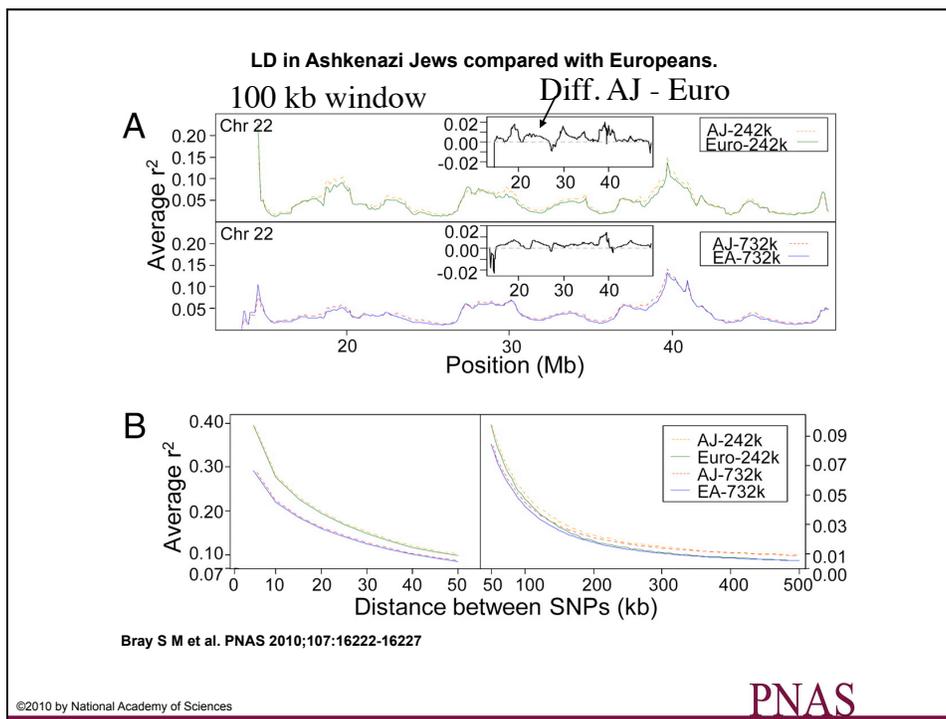
- Both Increase Frequency of Homozygotes Relative to Hardy-Weinberg (result in $f > 0$)
- Increased Homozygosity Under Assortative Mating Occurs Only For Loci Contributing to the Phenotype Or For Loci Correlated For Any Reason to the Phenotype; Inbreeding Increases Homozygosity for All Loci
- Neither Changes Allele Frequencies --Therefore They Are Not Evolutionary Forces at the Single Locus Level
- Assortative Mating Creates Disequilibrium Among Loci that Contribute to the Phenotype; Inbreeding Slows Down the Decay of Disequilibrium, but Does Not Create Any Disequilibrium.

ASSORTATIVE MATING, LINKAGE DISEQUILIBRIUM AND ADMIXTURE

- Assortative mating directly affects the genotype and gamete frequencies of the loci that contribute to the phenotype for which assortative mating is occurring and of any loci in linkage disequilibrium with them.
- **Admixture** occurs when two or more genetically distinct subpopulations are mixed together and begin interbreeding.
- Admixture induces disequilibrium, so assortative mating for any phenotype associated with the parental subpopulations can potentially affect the genotype frequencies at many loci not directly affect the assorting phenotype.

ASSORTATIVE MATING, LINKAGE DISEQUILIBRIUM AND ADMIXTURE

Subpopulation 1				Subpopulation 2			
AB	Ab	aB	ab	AB	Ab	aB	ab
0.03	0.07	0.27	0.63	0.63	0.27	0.07	0.03
$D = (0.03)(0.63) - (0.07)(0.27) = 0$				$D = (0.63)(0.03) - (0.27)(0.07) = 0$			
<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> </div> <div style="text-align: center;"> </div> </div>							
Combined Population (50:50 Mix)							
AB	Ab	aB	ab	AB	Ab	aB	ab
0.33	0.17	0.17	0.33	0.33	0.17	0.17	0.33
$D = (0.33)(0.33) - (0.17)(0.17) = 0.08$							



ASSORTATIVE MATING, LINKAGE DISEQUILIBRIUM AND ADMIXTURE

- Assortative mating for *any* trait that differentiates the original subpopulations (even non genetic) reduces heterozygosity at all loci with allele frequency differences between the original subpopulations.
- The rate of dissipation of D in the admixed population is therefore $< (1-r)$.
- The admixed populations do not fuse immediately, but rather remain stratified, sometimes indefinitely if the assortative mating is strong enough.

Disassortative Mating

occurs when individuals with dissimilar phenotypes are more likely to mate than expected under random pairing in the population

Disassortative Mating



Cowslip

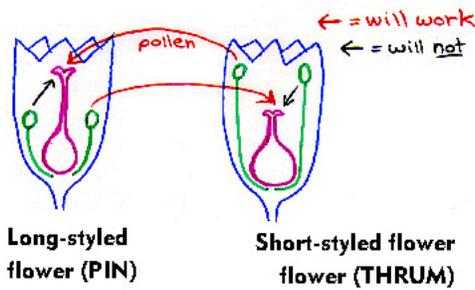
Disassortative Mating



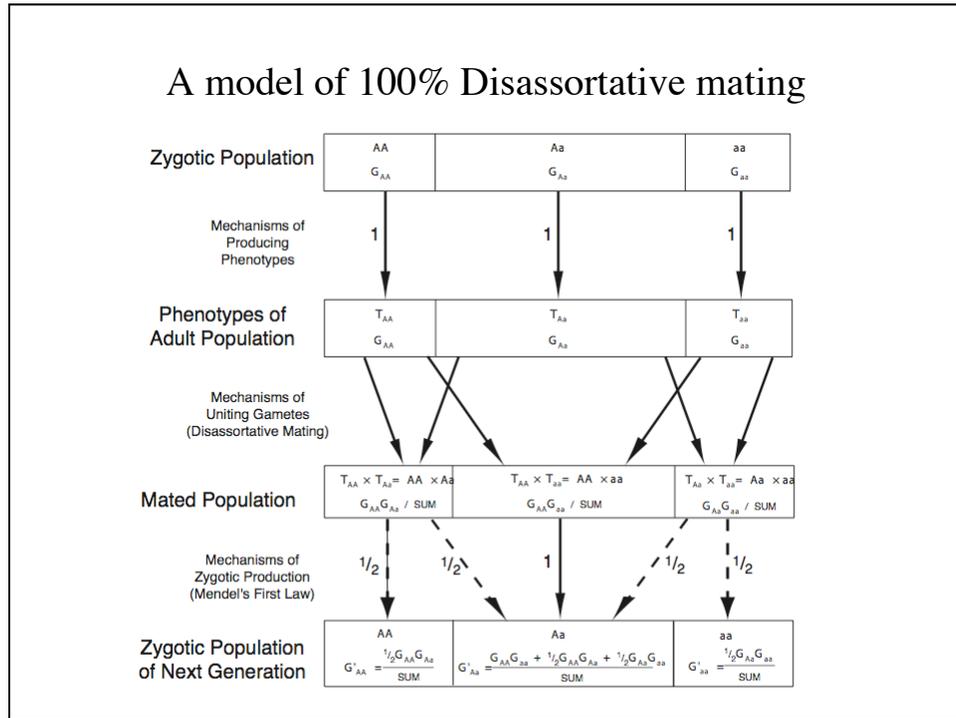
Cowslip

Disassortative Mating

Heterostyly – Two different types of perfect flowers, each type on a different plant



Cowslip



Disassortative Mating Starting at HW Equilibrium

generation	AA	Aa	aa	p	f
0	0.5625	0.3750	0.0625	0.7500	0.0000
1	0.3913	0.5652	0.0435	0.6739	-0.2860
2	0.4209	0.5324	0.0468	0.6871	-0.2380
3	0.4170	0.5366	0.0463	0.6853	-0.2442
4	0.4176	0.5361	0.0464	0.6856	-0.2434
5	0.4175	0.5361	0.0464	0.6855	-0.2435
6	0.4175	0.5361	0.0464	0.6856	-0.2435
7	0.4175	0.5361	0.0464	0.6856	-0.2435
8	0.4175	0.5361	0.0464	0.6856	-0.2435
9	0.4175	0.5361	0.0464	0.6856	-0.2435
10	0.4175	0.5361	0.0464	0.6856	-0.2435
11	0.4175	0.5361	0.0464	0.6856	-0.2435
12	0.4175	0.5361	0.0464	0.6856	-0.2435
13	0.4175	0.5361	0.0464	0.6856	-0.2435

Disassortative Mating Starting at HW Equilibrium

generation	AA	Aa	aa	p	f
0	0.0625	0.3750	0.5625	0.2500	0.0000
1	0.0435	0.5652	0.3913	0.3261	-0.2860
2	0.0468	0.5324	0.4209	0.3129	-0.2380
3	0.0463	0.5366	0.4170	0.3147	-0.2442
4	0.0464	0.5361	0.4176	0.3144	-0.2434
5	0.0464	0.5361	0.4175	0.3145	-0.2435
6	0.0464	0.5361	0.4175	0.3144	-0.2435
7	0.0464	0.5361	0.4175	0.3144	-0.2435
8	0.0464	0.5361	0.4175	0.3144	-0.2435
9	0.0464	0.5361	0.4175	0.3144	-0.2435
10	0.0464	0.5361	0.4175	0.3144	-0.2435
11	0.0464	0.5361	0.4175	0.3144	-0.2435
12	0.0464	0.5361	0.4175	0.3144	-0.2435
13	0.0464	0.5361	0.4175	0.3144	-0.2435

Note, the Equilibrium depends upon the starting conditions; multiple polymorphic equilibria are common with disassortative mating

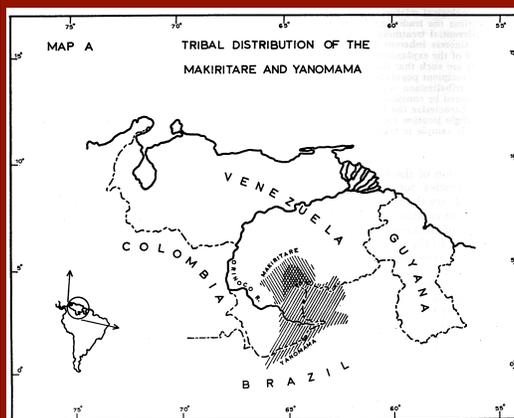
Disassortative Mating as an Evolutionary Force

- Is a powerful evolutionary force at the single locus level, generally resulting in stable equilibrium populations with intermediate allele frequencies and $f < 0$
- It is less powerful as an evolutionary force at the multi-locus level because it produces a heterozygote excess, which allows linkage disequilibrium to break down more rapidly
- Mimics the heterozygote excess of avoidance of inbreeding, but unlike avoidance of inbreeding, it affects only those loci correlated with the relevant phenotype, and it causes allele frequency change.

Disassortative Mating and Admixture

- Disassortative mating amplifies gene flow between the parental subpopulations.
- **Therefore, disassortative mating rapidly destroys genetic differences between historical subpopulations**
- Disassortative mating increases heterozygosity above random mating expectations for all loci with initial allele frequency differences between the parental subpopulations, and hence D dissipates at a rate $> (1-r)$.
- **Therefore, disassortative mating rapidly destroys the linkage disequilibrium created by admixture.**

Disassortative Mating and Admixture



Disassortative Mating and Admixture

Diagnostic Allele	Yanomama	Borabuk Yanomama	Makiritare
Di^a	0.00	0.06	0.04
Ap^a	0.00	0.08	0.05

Systems of Matings

Systems of mating can be potent evolutionary forces, both by themselves and in interactions with other evolutionary factors. In subsequent lectures we will examine additional interactions between system of mating and other evolutionary forces.