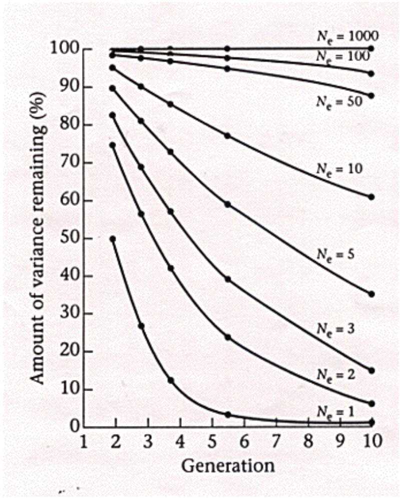
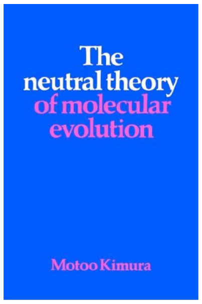
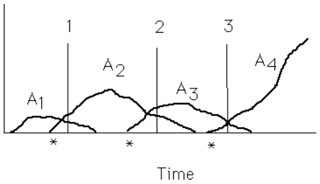
Genetic Drift & Inbreeding contd....



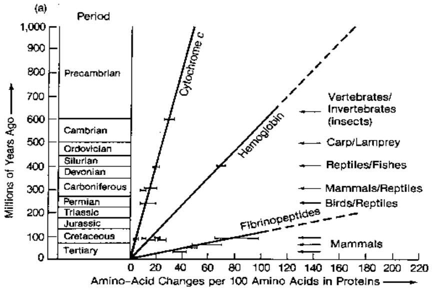
The rate of evolution by drift alone....



At a single locus
substitution = fixation of new mutation



- Novel mutation (AA subst) fixes every 2 yrs on av. (Kimura)
- Clocklike sequence evolution (Zuckerkandl & Pauling)



The rate at which two populations divergence (fix differences in DNA sequences) is $2tu_n$, where

t = time of last common ancestor
u_n= neutral mutation rate

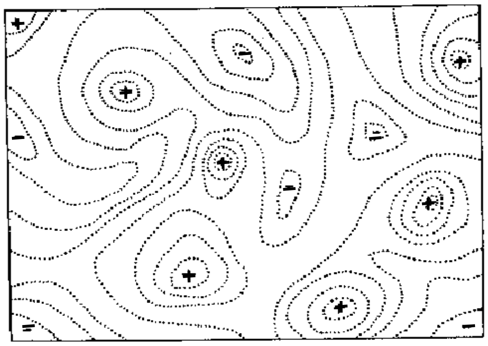
√ Pseudogenes
√ Silent substitutions > replacement substitutions

But
- Variation amongst loci is evidence of functional constraints
- Some proteins seq undergo clocklike change, irrespective of generation time

Currently:
- Serves as Null model
- Evidence is accumulating but most likely Neutral Theory is overstated

'The Shifting Balance' - Sewall Wright, 1931

Fitness surface/Adaptive landscape

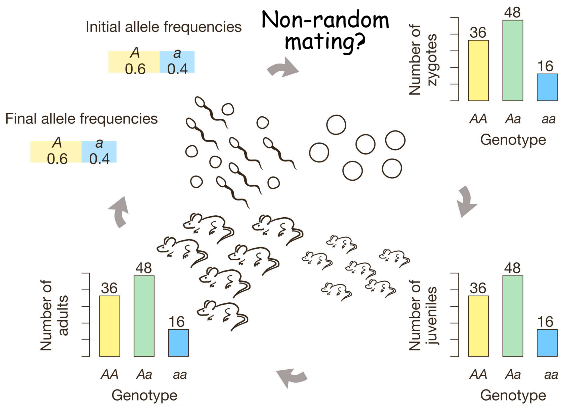


1: Drift **2: Selection** **3: Migration**

HW Assumptions

- No selection
- No mutation
- No migration
- No random events
- Pop. infinitely large, stable, with equal sex ratio
- Mating within population at random (panmixia)

Population genetic model



Mating Systems

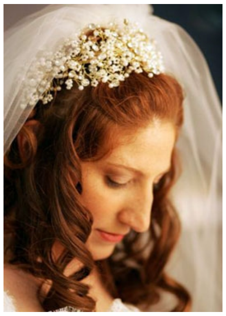
Random mating	mating independent of genotype or phenotype
Inbreeding	mating between relatives more common than expected by chance
Negative Inbreeding (enforced outbreeding)	mating between relatives less common than expected by chance
Assortative mating	
- Positive	bias towards mating with phenotypically similar partners
- Negative	bias towards mating with phenotypically dissimilar partners

Inbreeding & Assortative mating are different

Inbreeding -> mating with relatives (more similar resemblance on av., but not necessarily for any particular trait)

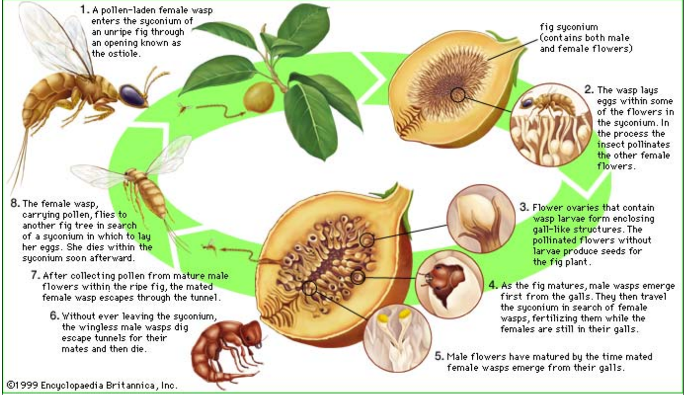
Assortative mating -> mating based on dis/similar traits; may/may not be relatives

e.g. humans



Inbreeding -> mating with relatives

e.g. Fig wasps



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Consequences of non-random mating

Inbreeding coefficient -> F

"probability that the two alleles within an individual are identical by descent (range 0-1)"

In a population…

- F = proportion of autozygous individuals (IBD)
- 1-F = proportion allozygous (identical by state; hom or het)

Calculating the Inbreeding coefficient (F)

Comparing observed & expected heterozygosities

$F = (H_{expected} - H_{observed}) / H_{expected}$

$H_{expected} = 2pq$

$H_{observed} = 2pq(1-F)$ (if F = 0, it is 2pq)

Consequences of non-random mating

H-W equilibrium: Δ in expected genotype freq

	AA	Aa	aa
F=0	p^2	$2pq$	q^2
0<F<1	$p^2(1-F)+pF$	$2pq(1-F)$	$q^2(1-F)+qF$
F=1	p	0	q

As long as F > 0, inbreeding will decrease heterozygosity

Example: Find p and F for a population with the following genotypic frequencies, AA 0.056, Aa 0.288, & aa 0.656.

First calculate p using genotypic frequencies:

Freq (A) = p = 0.056 + (0.288)/2 = 0.2
Freq (a)= q = 1- 0.2 = 0.8

Then estimate expected freq of hets (H) (based on H-W):

$H_{expected} = 2(0.2)(0.8) = 0.32$

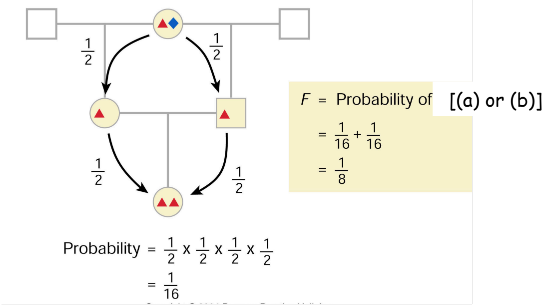
$\boxed{H_{observed} = 0.288}$

F can be obtained from the frequency of heterozygotes:

$F = (H_{expected} - H_{observed}) / H_{expected}$

$F = (0.32 - 0.288) / 0.32 = \boxed{0.1}$

◆ Calculating the inbreeding coefficient F from a pedigree



Change of inbreeding coefficient over time:

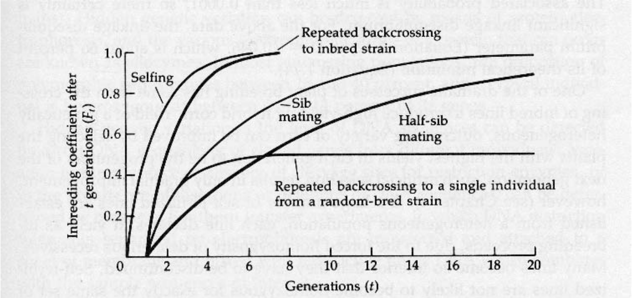


Figure 24. Theoretical increase in inbreeding coefficient F for regular systems of mating: selfing, sib mating, half-sib mating, and repeated backcrossing.

- approaches 1 over generations
- rate depends on mating system

Consequences of non-random mating:

- **no** change in allele freq, but change in genotypic freq.
- Genetic variance of phenotypic character increases
- Promotes linkage disequilibrium
- Inbreeding depression - uncovering deleterious recessives

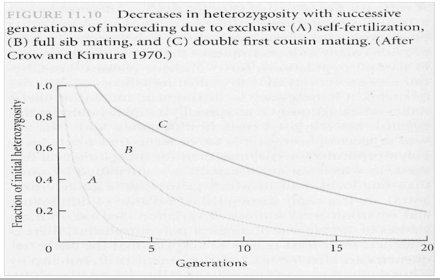
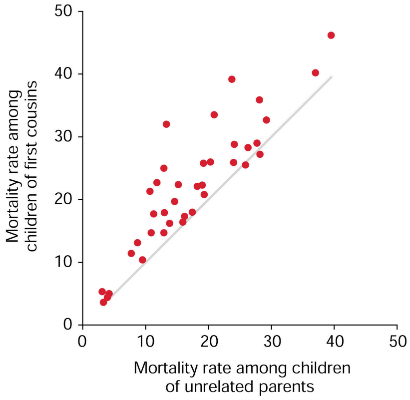


FIGURE 11.10 Decreases in heterozygosity with successive generations of inbreeding due to exclusive (A) self-fertilization, (B) full sib mating, and (C) double first cousin mating. (After Crow and Kimura 1970.)

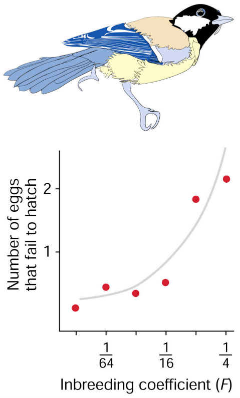
Inbreeding depression in humans

Mortality rates in:	**Period**	**Children of first cousins**	**Children of non-relatives**
Young children (US)	< 1858	22%	16%
Children <20 (US)	18th-19thC.	17%	12%
Children <10 (US)	1920-1956	8.1%	2.4%
Children <1 (France)	1919-1950	9.3%	3.9%
Children (France)	1919-1950	14%	10%

Inbreeding depression among humans



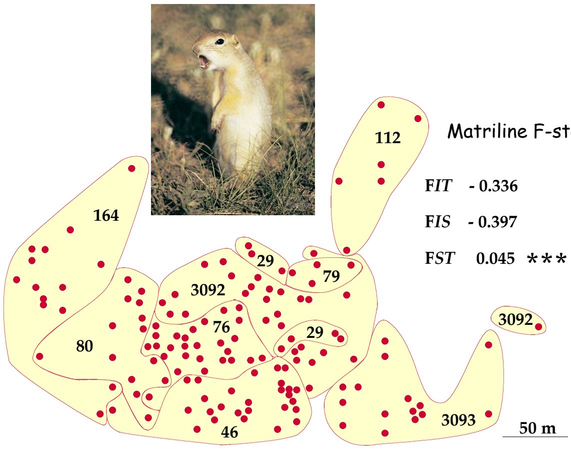
Inbreeding depression in birds (Parus major)



Inbreeding….
its not all bad!

- Male dispersal
- Female philopatry
- Synchronized estrous

What are the genetic consequences?
Significance?



Matriline F-stats

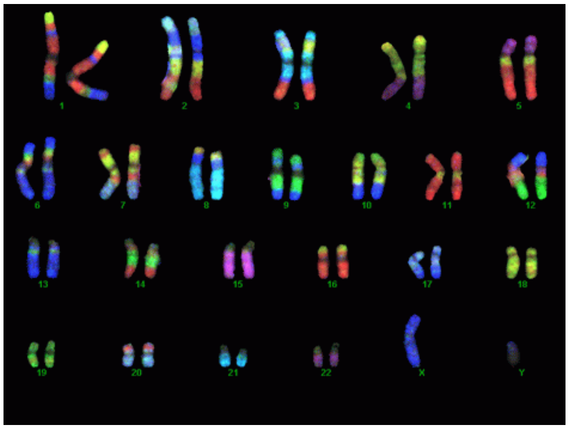
FIT - 0.336
FIS - 0.397
FST 0.045 ***

Inbreeding in nature....   not uncommon

Inbreeding avoidance:
Plants - separate sexes (dioceous)
- morphological alterations of hermaphrodites
- self incompatibility alleles

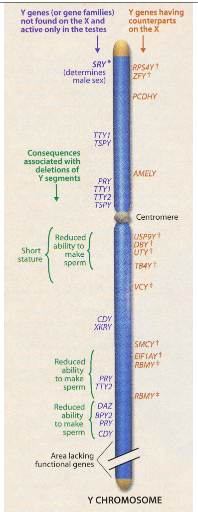
Animals - dispersal
- delayed reproduction
- kin recognition (& mate choice)

A case study in linkage disequilibrium: the Y



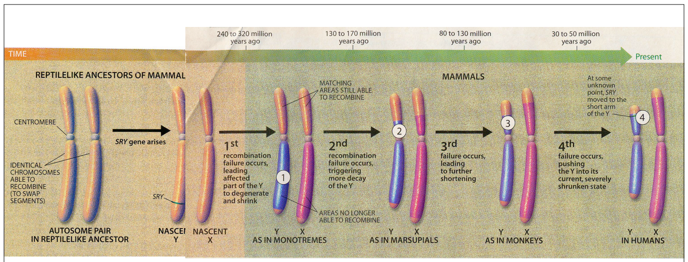
Evidence

- Tips recombine at meiosis in males
- NRY genes have counterparts on X
- Stepwise loss of recombination in Y (sequenced 19 genes in NRY of X and Y)



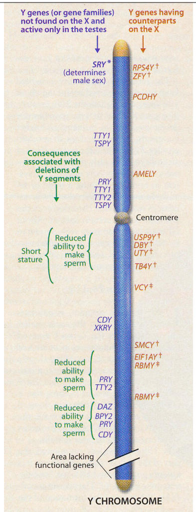
† housekeeping genes

NRY



Monotremes (platypus, echidna)	Marsupials	Placental mammals	Apes & Hominids

- Inversion
- 4 grps of seq diff.
- Cross-spp comparison
- starting ca. SRY origin, 300 mya (sex-determining region Y > protein triggers formation testes)
- Molecular clock



NRY

† housekeeping genes

1. Recombination failure
2. Degeneration
3. Compensation

(double X activity in males; double X in fe/males & 1/2 f; X inactivation)

! Magnet for acquisition of fertility genes

! avoid degeneration (multiple copies)