

Lecture 7

Decay of LD in a very large boring
randomly mating population

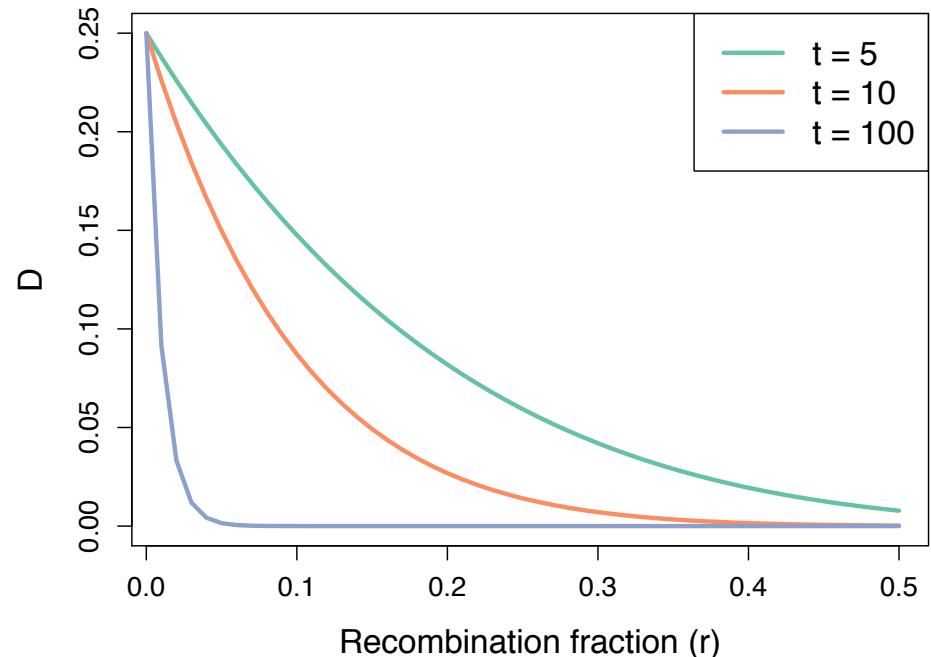
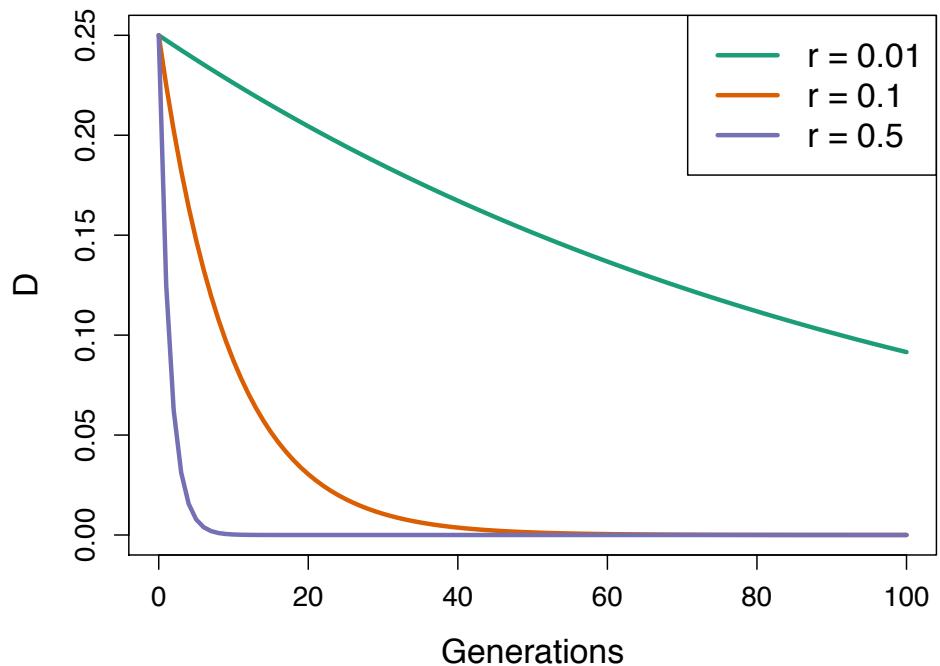
$$D_t = (1 - r)^t D_0$$

With inbreeding coefficient f replace r with $r(1-f)$

linkage disequilibrium

How does LD change over time due to recombination?

$$D_t = (1 - r)^t D_0$$



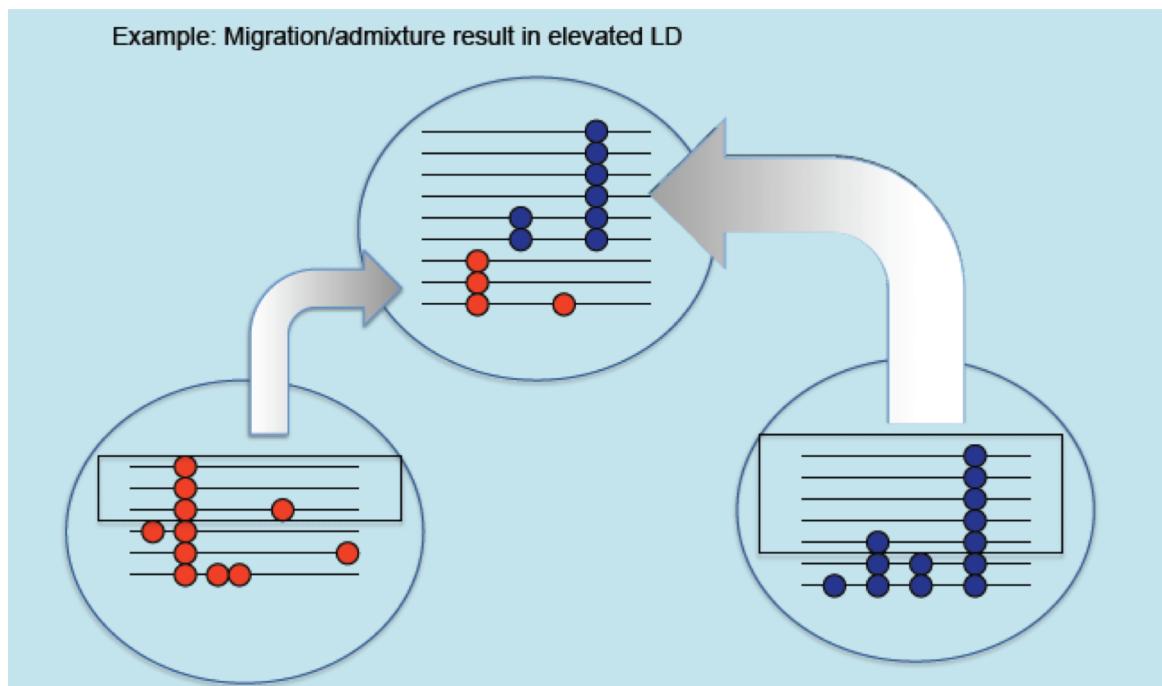
So eventually recombination leads to $D=0$. Even with free recombination ($r=0.5$), it isn't instantaneous however.

What creates LD

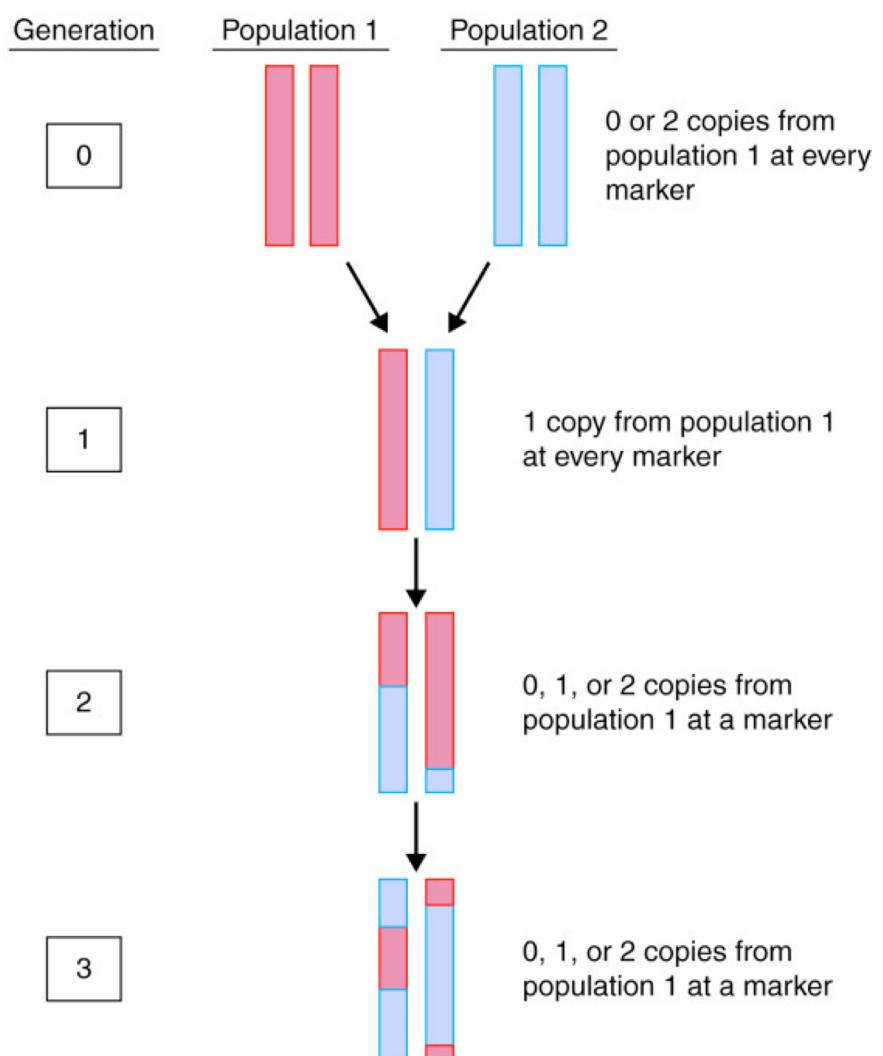
- Mutational origin
- Genetic drift (and Hitchhiking)
- Epistatic selection*
- Assortative mating.
 - Inbreeding
 - Population structure and admixture
 - Assortative mating by phenotype*
- *only for specific markers

Countervailing forces that increase LD

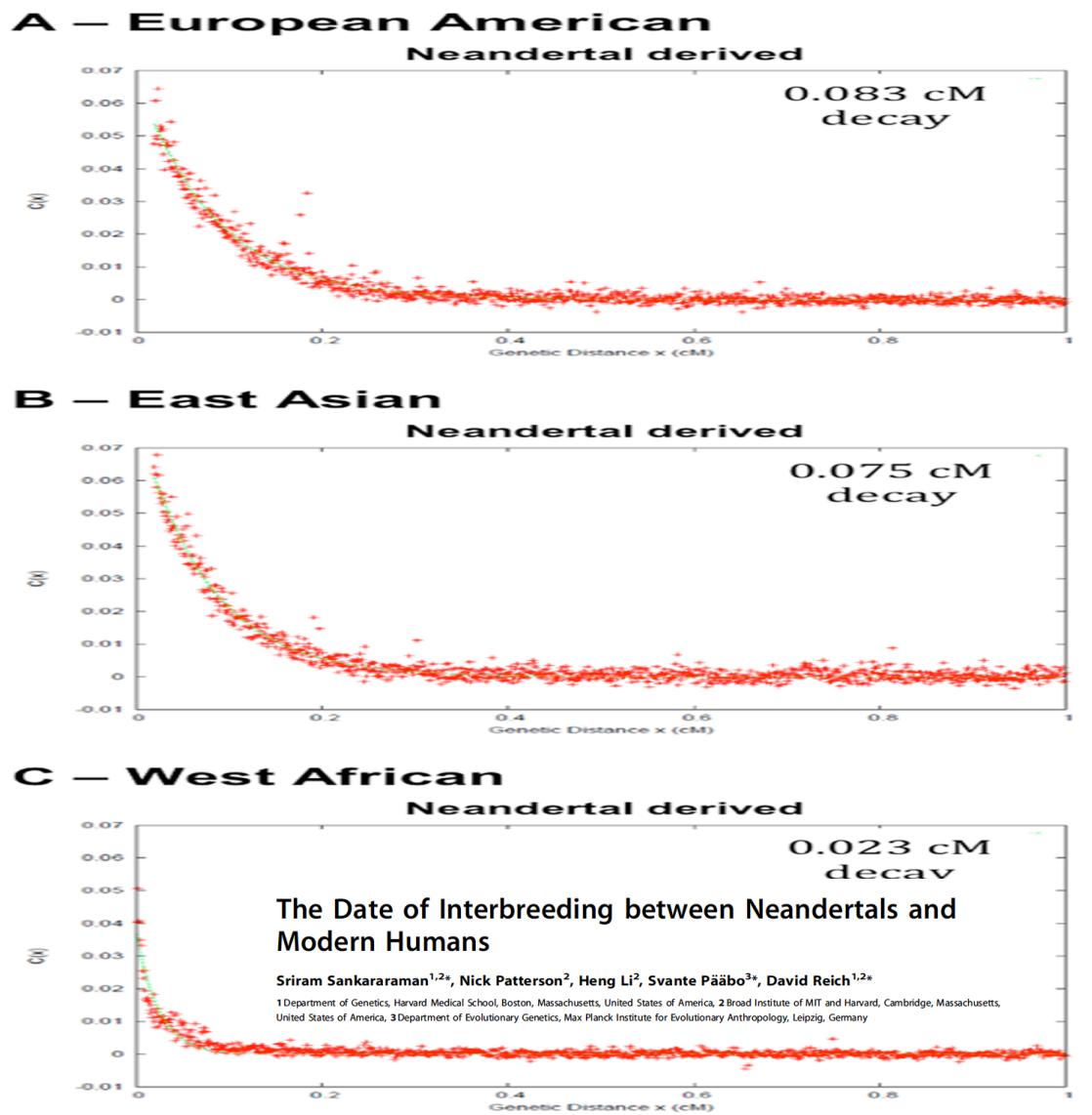
Population structure can increase LD if allele frequencies differ among populations



Pretty pictures courtesy of P. Andolfatto (Princeton)



LD between Neanderthal alleles in modern human populations



Evolution by genetic drift

- **Evolution by Genetic drift:** a change in allele frequency because individuals carry the allele by chance produce more / less offspring in any given generation. *
- *in sexual populations....
 - Genetic drift can affect selected alleles but only if they are very weakly selected (except when they are rare).
 - A neutral allele: An allele with no effect on fitness from other alleles at that locus.

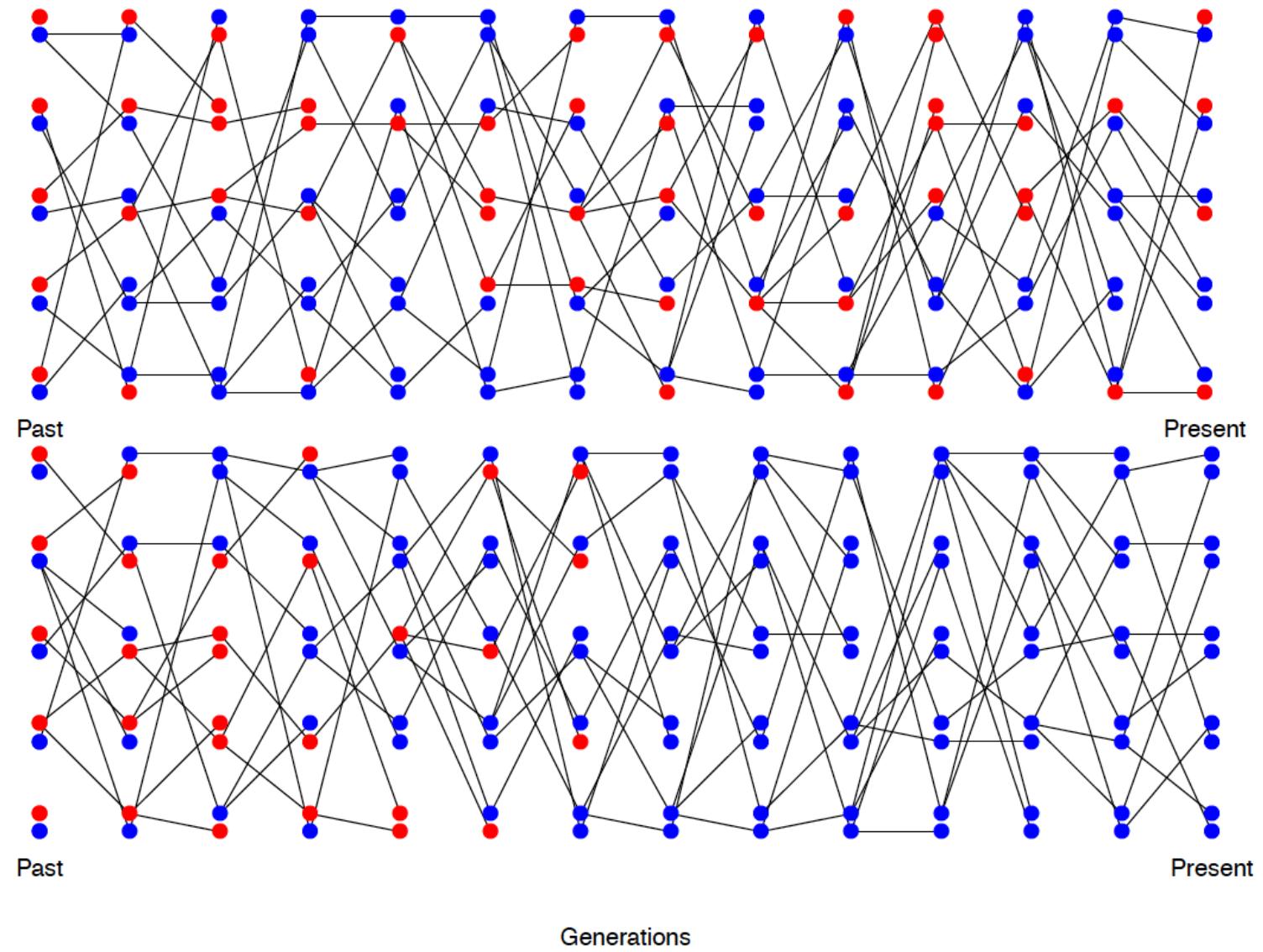
Neutral theory of molecular evolution

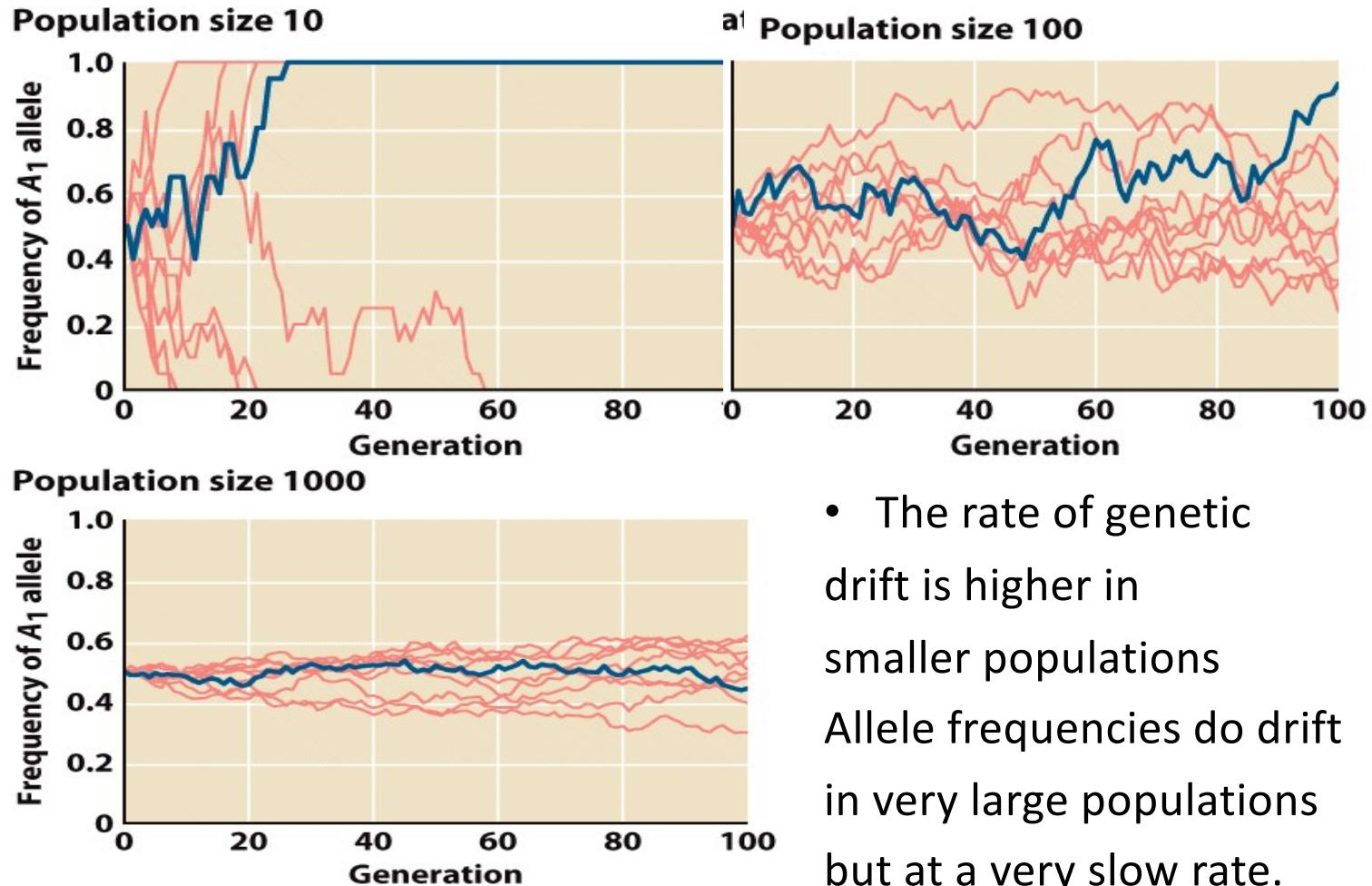
- Kimura 1968; King and Jukes 1969
- Claimed:
 - Most new mutations are deleterious and are lost immediately
 - Most of the observed molecular polymorphism and substitutions are neutral



Claimed that this is consistent with:

- High levels of genetic polymorphism
- The molecular clock





- The rate of genetic drift is higher in smaller populations
- Allele frequencies do drift in very large populations but at a very slow rate.

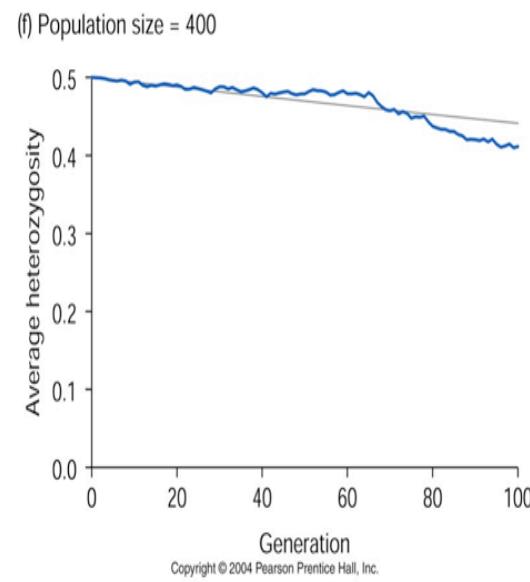
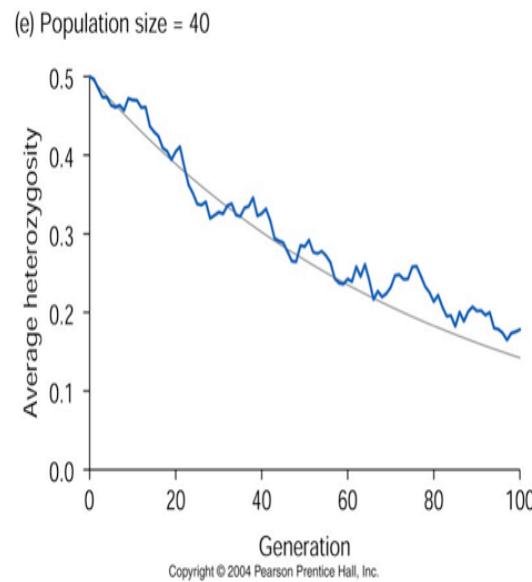
Evolution, 1/e Figure 8.3

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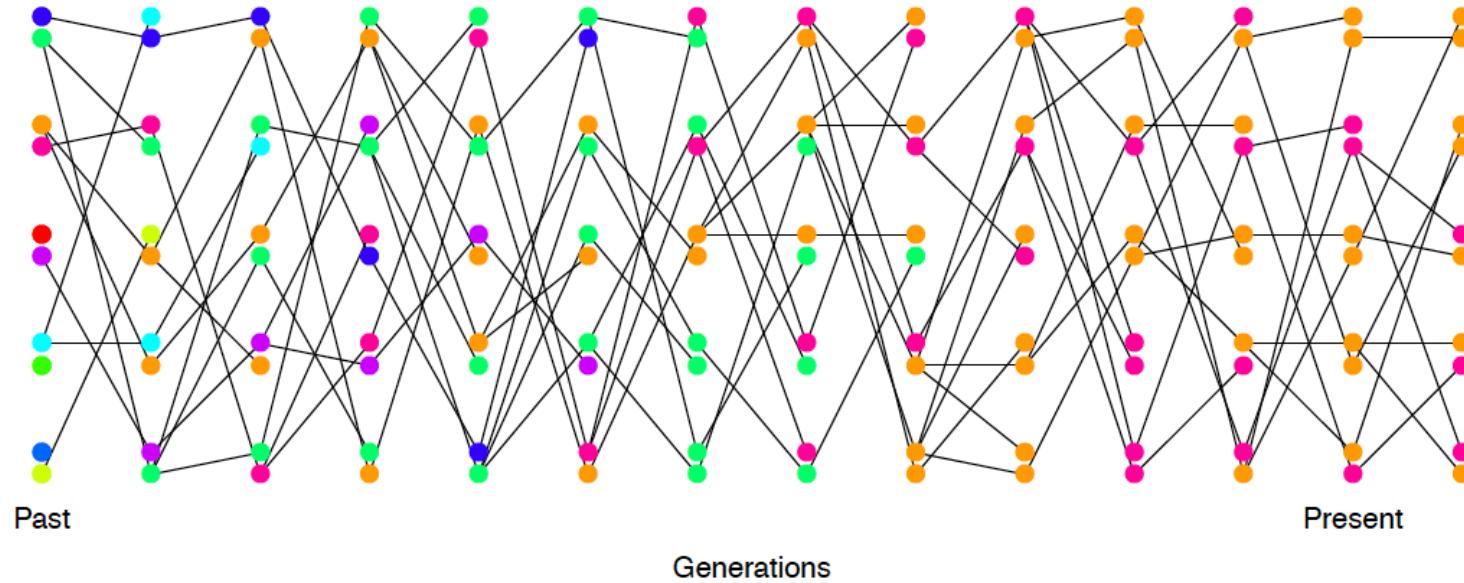
Loss of heterozygosity

- In the absence of new mutations, alleles drift to either loss or fixation. Thus the amount of heterozygosity within the population decreases at a rate inversely proportional to population size

Heterozygosity =
Fraction of sites that
are heterozygous



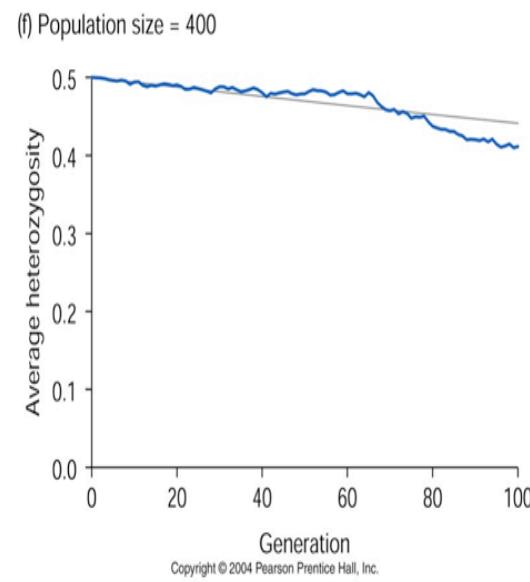
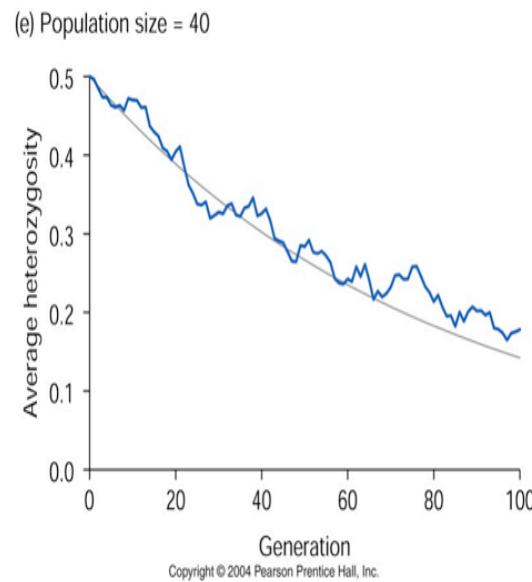
Loss of heterozygosity



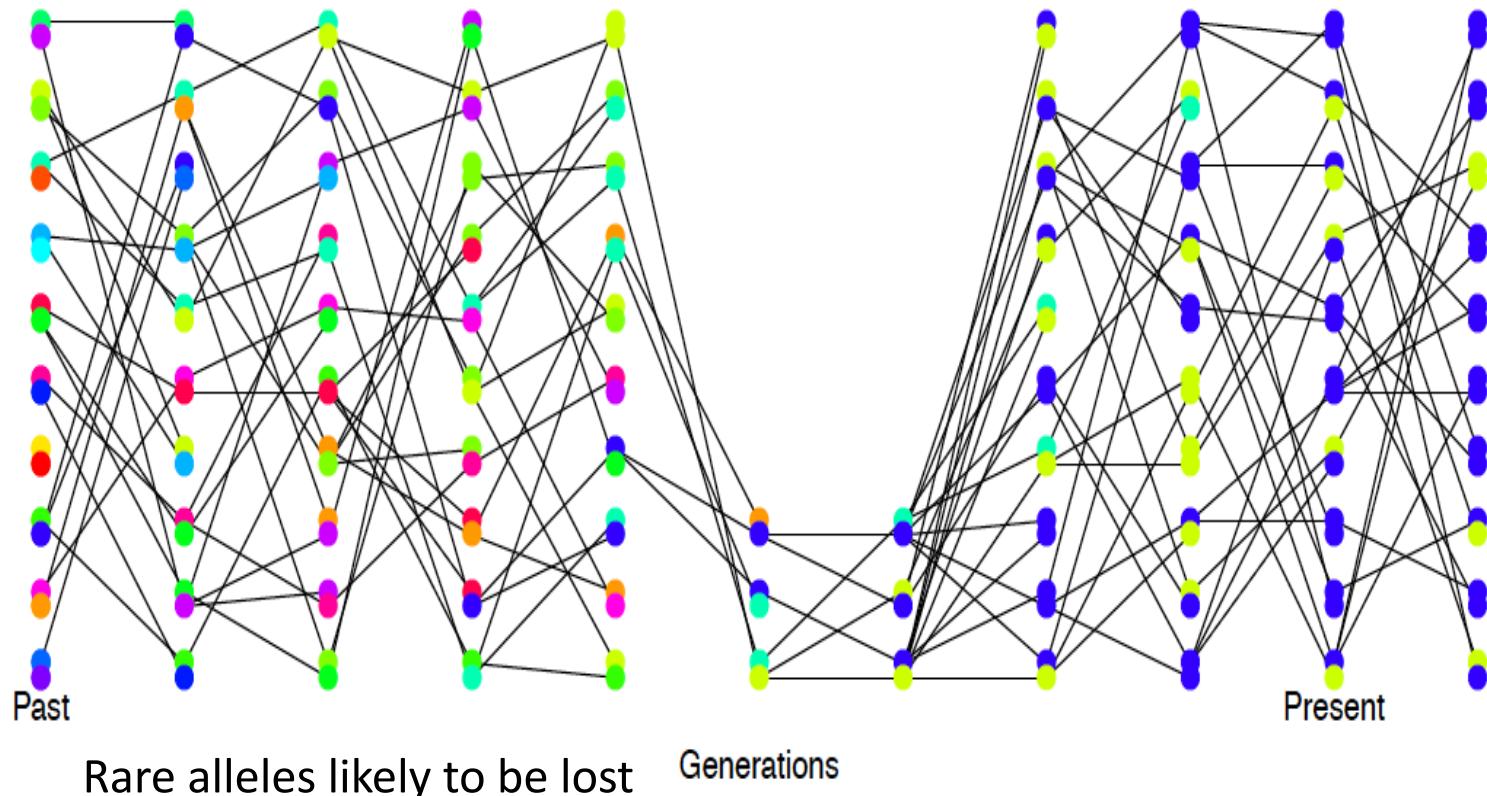
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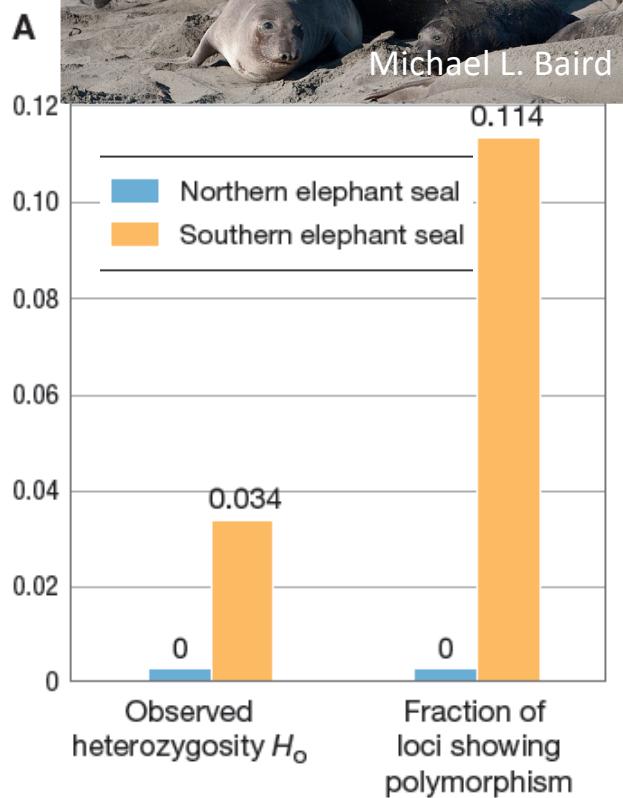
Heterozygosity =
Fraction of sites that
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- Profound effects of short-term reduction in population size.
- The effect of population bottlenecks (founder effects) on polymorphism

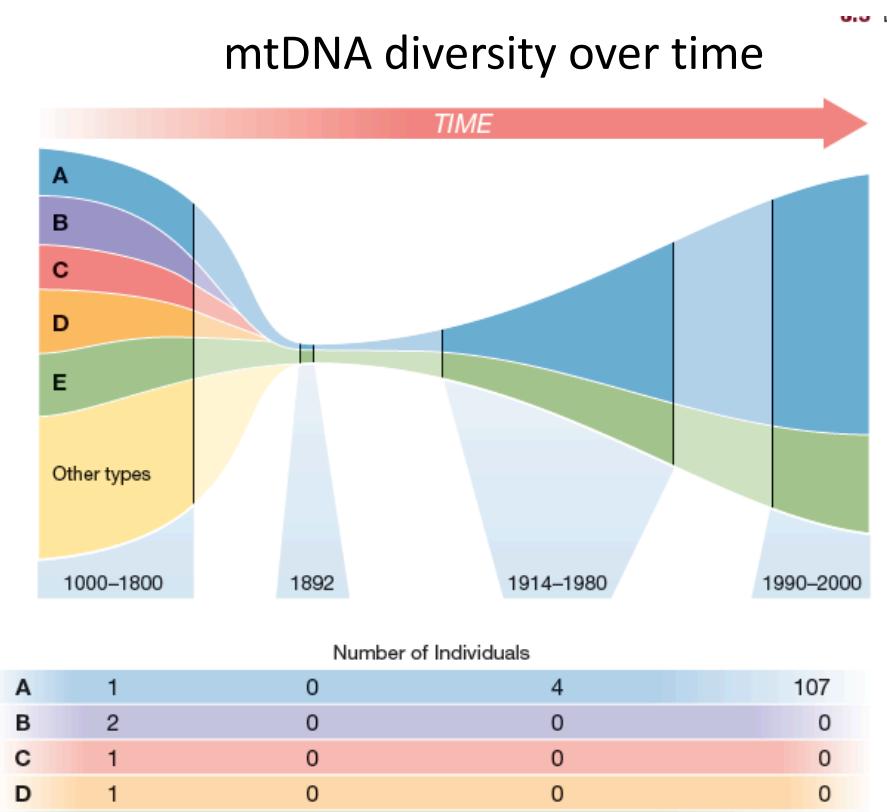


But some rare alleles can by chance drift to high frequency within the population.

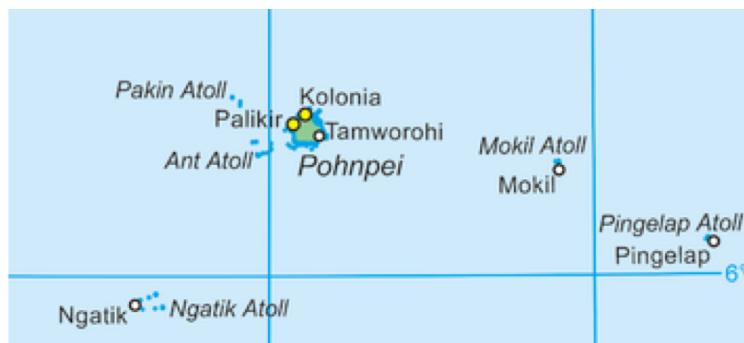


Bottleneck in Northern Elephant Seals

Figures from Bergstrom and Dugatkin. Evolution. 2nd Ed



During bottlenecks rare alleles can by chance reach high frequency



5% of islanders on Pingelap have
A recessive form of achromatopsia
(total colour blindness)
The allele is at ~20% frequency



Higher incidence of polydactyl in Amish population

Using Genetic Tests, Ashkenazi Jews Vanquish a Disease

By GINA KOLATA
Published: February 18, 2003

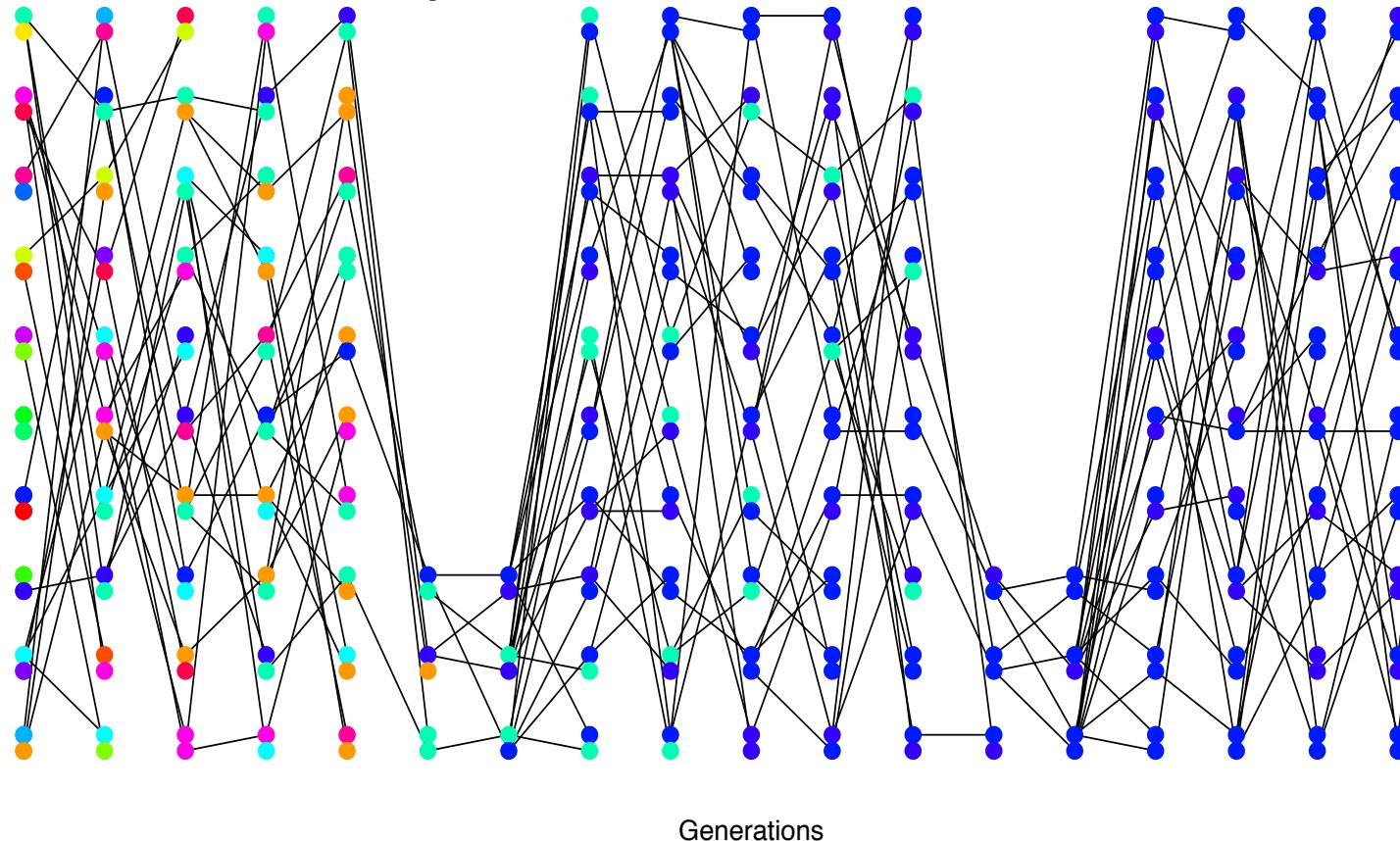
A number of years ago, five families in Brooklyn who had had babies with a devastating disease decided to try what was then nearly unthinkable: to eliminate a terrible genetic disease from the planet.

The disease is Tay-Sachs, a progressive, relentless neurological disorder that afflicts mostly babies, leaving them mentally impaired, blind, deaf and unable to swallow. There is no treatment, and most children with the disease die by 5.

- SIGN RECC
 - TWIT!
 - SIGN E-MAI
 - PRINT
 - SING!
- JustWri

Tay-Sachs disease (a recessive disorder) is found at higher frequency in Ashkenazi Jews

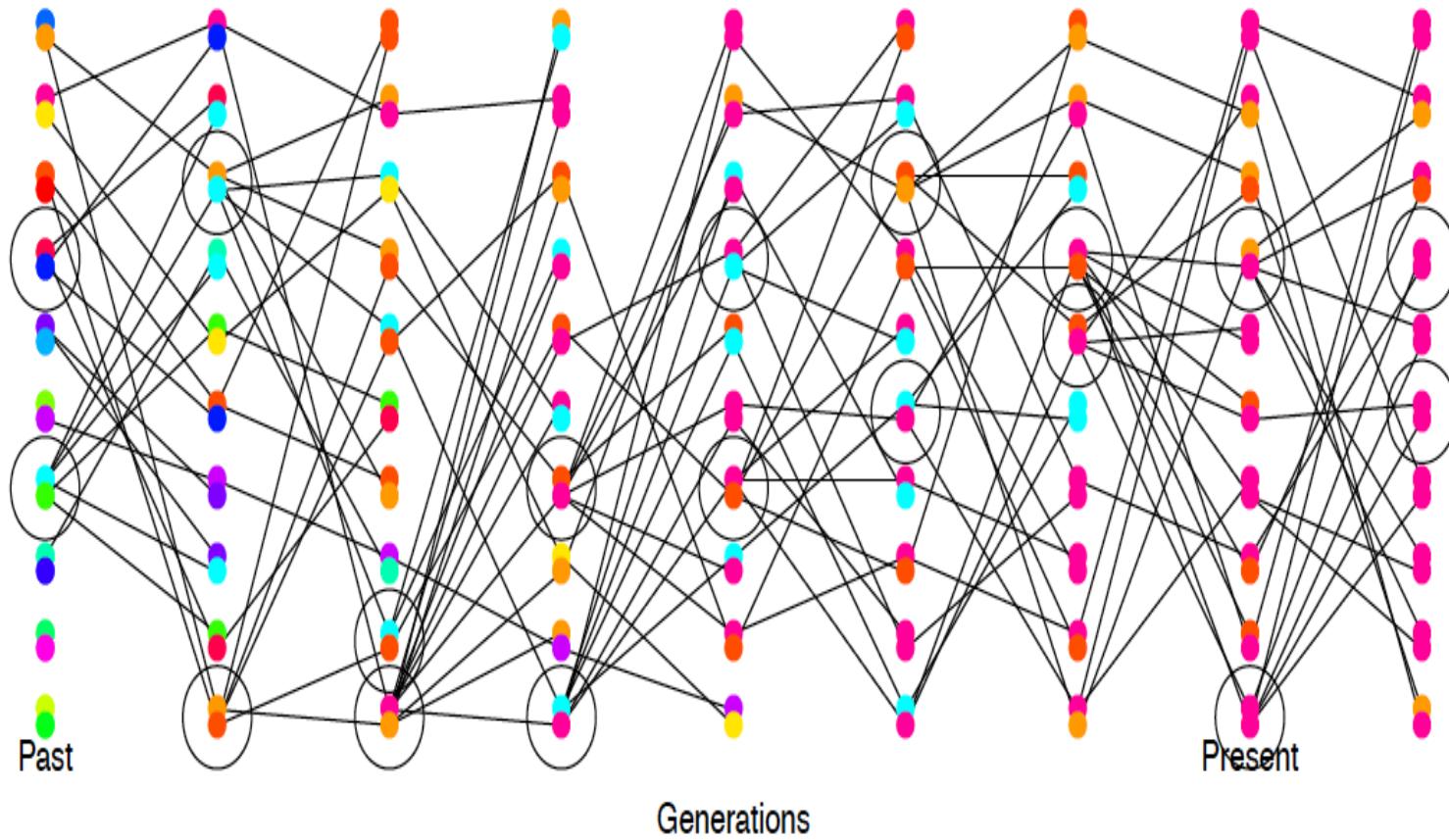
Effective Population size



- If the population often crashes to a small size = rate of drift is higher

Effective Population size

- higher variance in reproductive success = rate of drift higher



Circled individuals have much higher reproductive success (independent of genotype at locus).

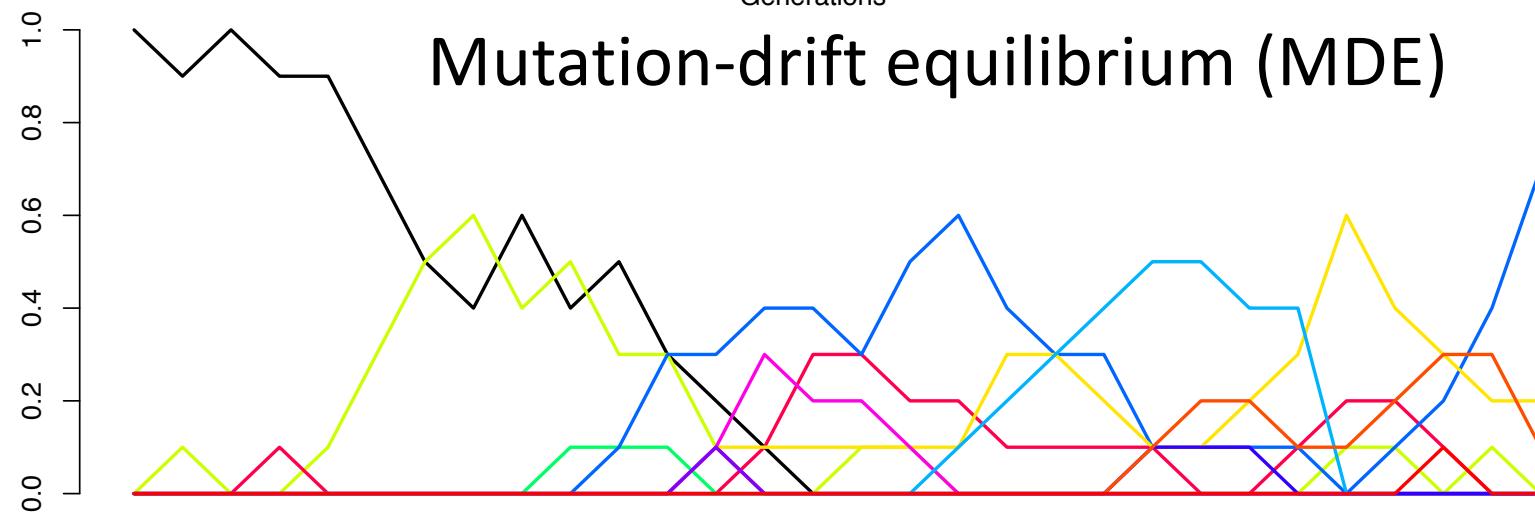
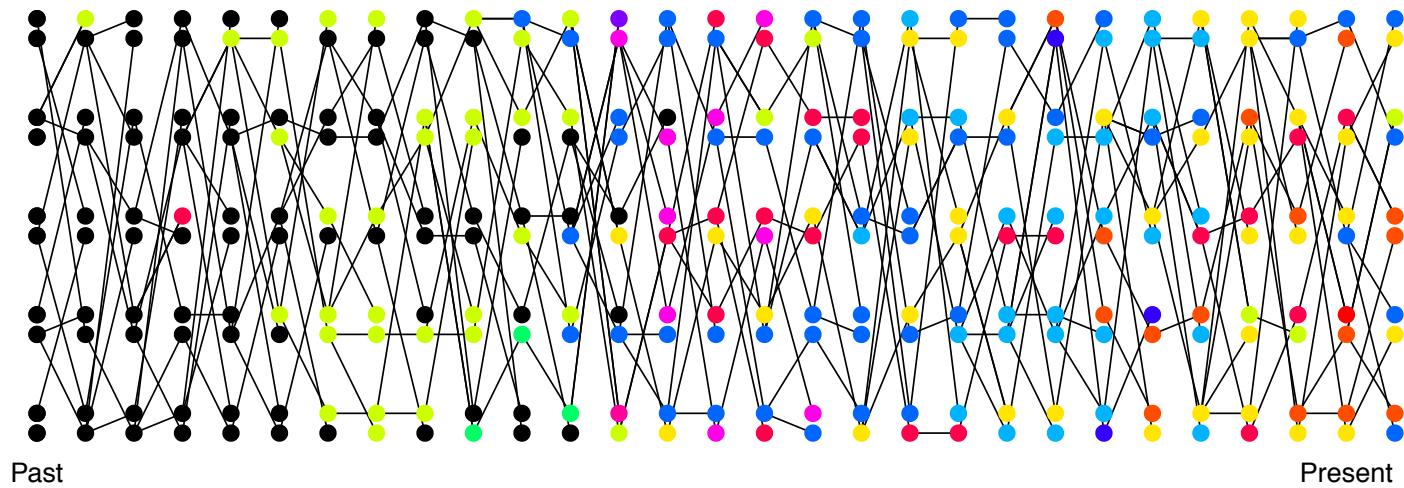
Effective Population size

Real populations deviate from many of the assumptions model (even ignoring selection, population structure).

- The rate of genetic drift, i.e. loss of heterozygosity, will be increased if:
 - The population often crashes to a small size
 - Or if there is a high variance in reproductive success.
- The effective population size N_e
 - The size of an ideal population in which drift occurs at the same rate as that in an actual population

$$N_e \ll N$$

In many (not all) situations, departures from model assumptions can be captured by substituting N_e for N , i.e., by plugging in a fictitious N that leads to the same level of genetic drift as observed.



Mutation-drift equilibrium (MDE)

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- Variation lost by drift = variation introduced by mutation
- N_e = effective population size,
 μ = mutation rate to new neutral alleles

At MDE, heterozygosity = $H \approx 4 N_e \mu$

The rate of genetic drift is slower in larger populations and the input of new mutations is higher. Large populations have a higher level of neutral polymorphism