

## II. Population Genetics

# Linkage Disequilibrium

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### Lecture 10

Instructor: Su-In Lee

## Summary of Last Lecture

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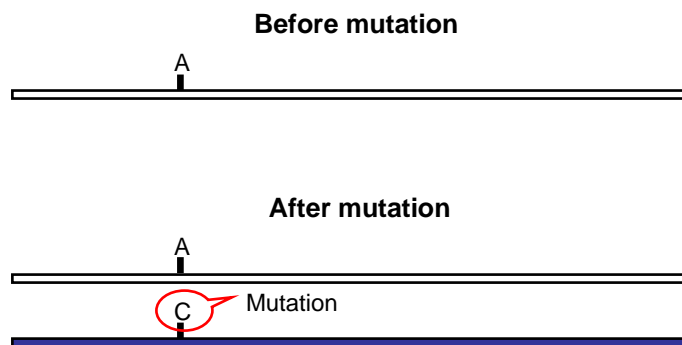
- Basic properties of a locus
  - Allele Frequencies
  - Genotype Frequencies
- Hardy-Weinberg Equilibrium
  - Relationship between allele and genotype frequencies that holds for most genetic markers
- Exact Tests for Hardy-Weinberg Equilibrium

## Today's Lecture

- Properties of pairs of alleles
- Haplotype frequencies
- Linkage equilibrium
- Linkage disequilibrium

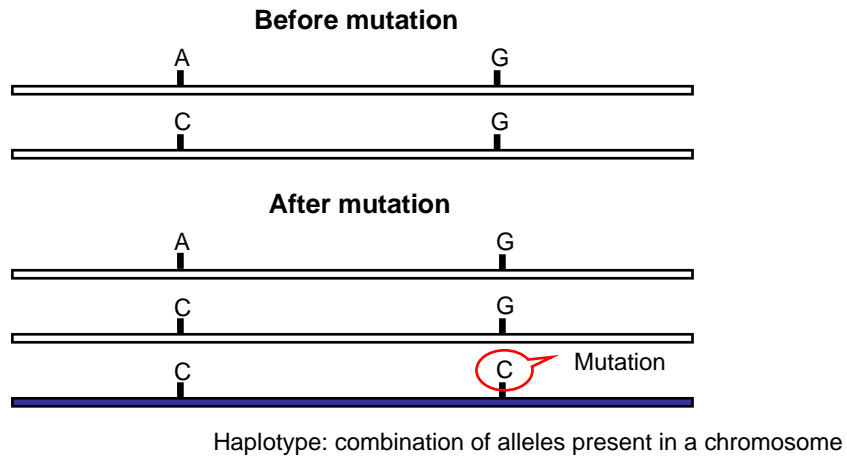
## History of two neighboring alleles

- Alleles that exist today arose through ancient mutation events...



## History of two neighboring alleles

- One allele arose first, and then the other...

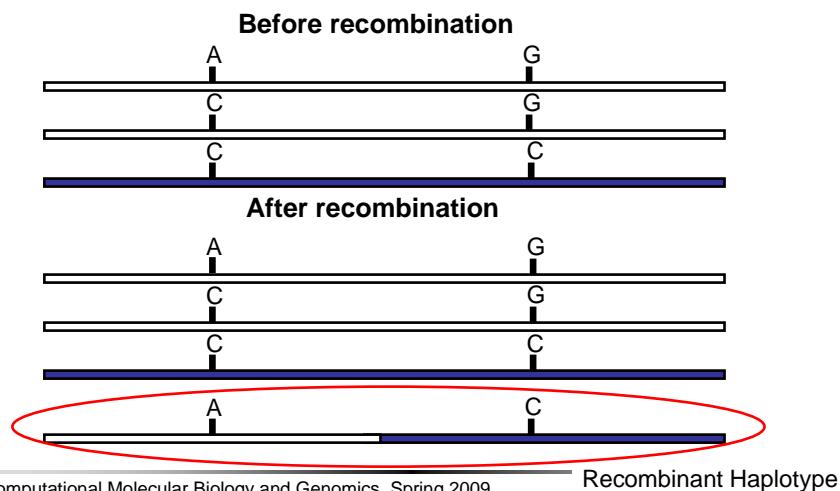


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## History of two neighboring alleles

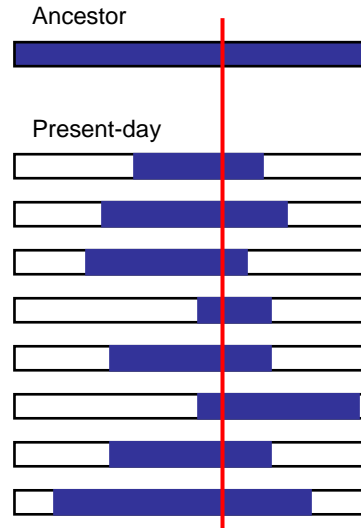
- Recombination generates new arrangements for ancestral alleles...



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## Linkage Disequilibrium (LD)

- Chromosomes are mosaics
- Extent and conservation of mosaic pieces depends on
  - Recombination rate
  - Mutation rate
  - Population size
  - Natural selection
- Combinations of alleles at very close markers reflect ancestral haplotypes

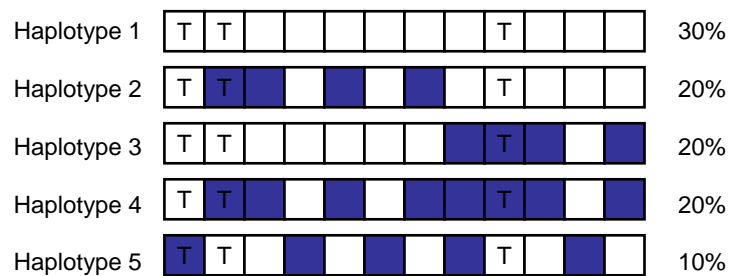


## Association Studies and Linkage Disequilibrium

- Why is LD important for gene mapping?
- If all polymorphisms were independent at the population level, association studies would have to examine every one of them...
- Linkage disequilibrium makes tightly linked variants strongly correlated producing cost savings for association studies

## Tagging SNPs

- In a typical short chromosome segment, there are only a few distinct haplotypes
- Carefully selected SNPs can determine status of other SNPs



## Basic Descriptors of Linkage Disequilibrium

## Commonly Used Descriptors

- Haplotype Frequencies
  - The frequency of each type of chromosome
  - Contain all the information provided by other summary measures
  
- Commonly used summaries
  - D
  - D'
  - $r^2$  or  $\Delta^2$

## Haplotype Frequencies

	<u>Locus B</u>		Totals
	<i>B</i>	<i>b</i>	
<u>Locus A</u>	<i>A</i>	$p_{AB}$ $p_{Ab}$	$p_A$
	<i>a</i>	$p_{aB}$ $p_{ab}$	$p_a$
Totals		$p_B$ $p_b$	1.0

## Linkage Equilibrium

- Expected for distant Loci...

$$p_{AB} = p_A p_B$$

$$p_{Ab} = p_A p_b = p_A(1 - p_B)$$

$$p_{aB} = p_a p_B = (1 - p_A)p_B$$

$$p_{ab} = p_a p_b = (1 - p_A)(1 - p_B)$$

## Linkage Disequilibrium

- Expected for nearby Loci...

$$p_{AB} \neq p_A p_B$$

$$p_{Ab} \neq p_A p_b = p_A(1 - p_B)$$

$$p_{aB} \neq p_a p_B = (1 - p_A)p_B$$

$$p_{ab} \neq p_a p_b = (1 - p_A)(1 - p_B)$$

## Disequilibrium Coefficient $D_{AB}$

$$D_{AB} = p_{AB} - p_A p_B$$

$$p_{AB} = p_A p_B + D_{AB}$$

$$p_{Ab} = p_A p_b - D_{AB}$$

$$p_{aB} = p_a p_B - D_{AB}$$

$$p_{ab} = p_a p_b + D_{AB}$$

## Acknowledgement

- This lecture note is based on material by Prof Goncalo Abecasis (Univ of Michigan).
- Chapter 2 of *Principles of Population Genetics* by Daniel L. Hartl & Andrew Clark