Selection at Two Loci

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Model with random mating, no selection

$$
\begin{aligned}
x_1 &= \text{frequency of } AB\text{-gametes} \\
p_A &= \text{frequency of } A\text{-gametes} \\
p_B &= \text{frequency of } B\text{-gametes} \\
c &= \text{probability of recombination}
\end{aligned}
$$

Change in frequency of AB-gametes during one generation:

$$x_1' = x_1 - cD$$

All four gametes, still no selection

Gamete		Recurrence	
AB	x_1'	$=$	$x_1 - cD$
Ab	x_2'	$=$	$x_2 + cD$
aB	x_3'	$=$	$x_3 + cD$
ab	x_4'	$=$	$x_4 - cD$

Selection affecting gametes

Gamete		Recurrence	
AB	x_1'	$=$	$w_1(x_1 - cD)/\bar{w}$
Ab	x_2'	$=$	$w_2(x_2 + cD)/\bar{w}$
aB	x_3'	$=$	$w_3(x_3 + cD)/\bar{w}$
ab	x_4'	$=$	$w_4(x_4 - cD)/\bar{w}$

where $\bar{w} = \sum x_i w_i$ is mean fitness.

What if selection acts on adults?

The effect of recombination

What gametes are produced by the following genotypes?

Genotype	Heterozygous loci	Gametes produced			
		AB	Ab	aB	ab
AB/AB	0	1			
AB/Ab	1	1/2	1/2		
AB/ab	2	$\frac{1-c}{2}$	$\frac{c}{2}$	$\frac{c}{2}$	$\frac{1-c}{2}$
Ab/aB	2	$\frac{c}{2}$	$\frac{1-c}{2}$	$\frac{1-c}{2}$	$\frac{c}{2}$

Only double heterozygotes make recombinant gametes.

If these genotypes have low fitness, few recombinants appear.
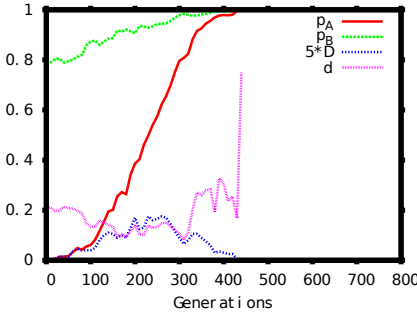
Selection affecting diploid adults

Gamete		Recurrence	
AB	x_1'	$=$	$\bar{w}_1(x_1 - cw_hD)/\bar{w}$
Ab	x_2'	$=$	$\bar{w}_2(x_2 + cw_hD)/\bar{w}$
aB	x_3'	$=$	$\bar{w}_3(x_3 + cw_hD)/\bar{w}$
ab	x_4'	$=$	$\bar{w}_4(x_4 - cw_hD)/\bar{w}$

▶ Fitnesses become $\bar{w}_i$: weighted mean over genotypes in which gamete i appears.
▶ Recombination limited by the fitness (w_h) of double heterozygotes: only these contribute recombinant gametes.
▶ Useful as a recipe for calculation.
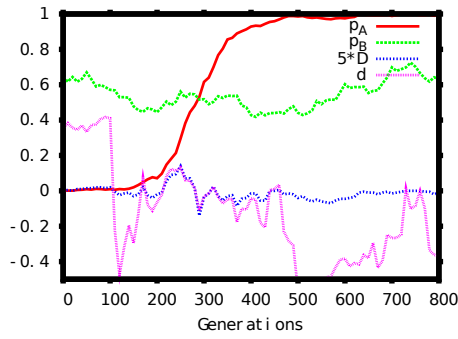
A sweeps; B hitch-hikes

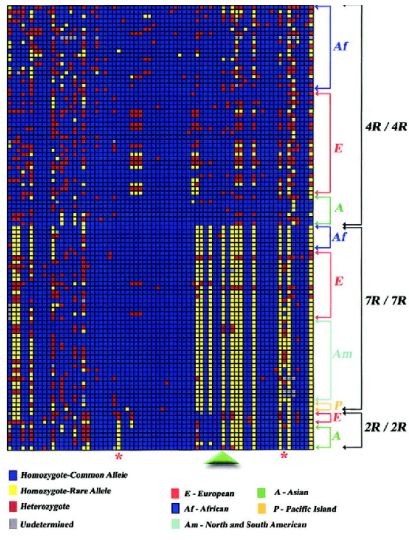Parameters: $s = 0.02$, $c = 0.001$, $N = 5000$

Selective sweep of allele A.

Allele B hitch-hikes to fixation.

D high when p_A has high heterozygosity.

d high throughout

Linked allele may fail to increase

Parameters: $s = 0.02$, $c = 0.001$, $N = 5000$

Allele A sweeps to fixation.

Little change in linked allele. Why?

LD lost early on this run, so D near 0.

Loss of LD shows as big drop in d.

- ▶ LD at D4 dopamine receptor
- ▶ Rows are diploid genotypes
- ▶ Blue: common homozygote
- ▶ Yellow: rare homozygote
- ▶ Red: heterozygote
- ▶ Note LD w/i 7R genotypes

DNA sequences from region of human lactase gene

Summary

- ▶ Two-locus gametic selection is very simple.
- ▶ When selection acts on diploids, the recombination rate is weighted by the fitness of double heterozygotes.
- ▶ Hitch-hiking: selection at one locus may change allele frequencies at linked loci.
- ▶ If enough recombination happens early in the process, linked loci do not hitch-hike.