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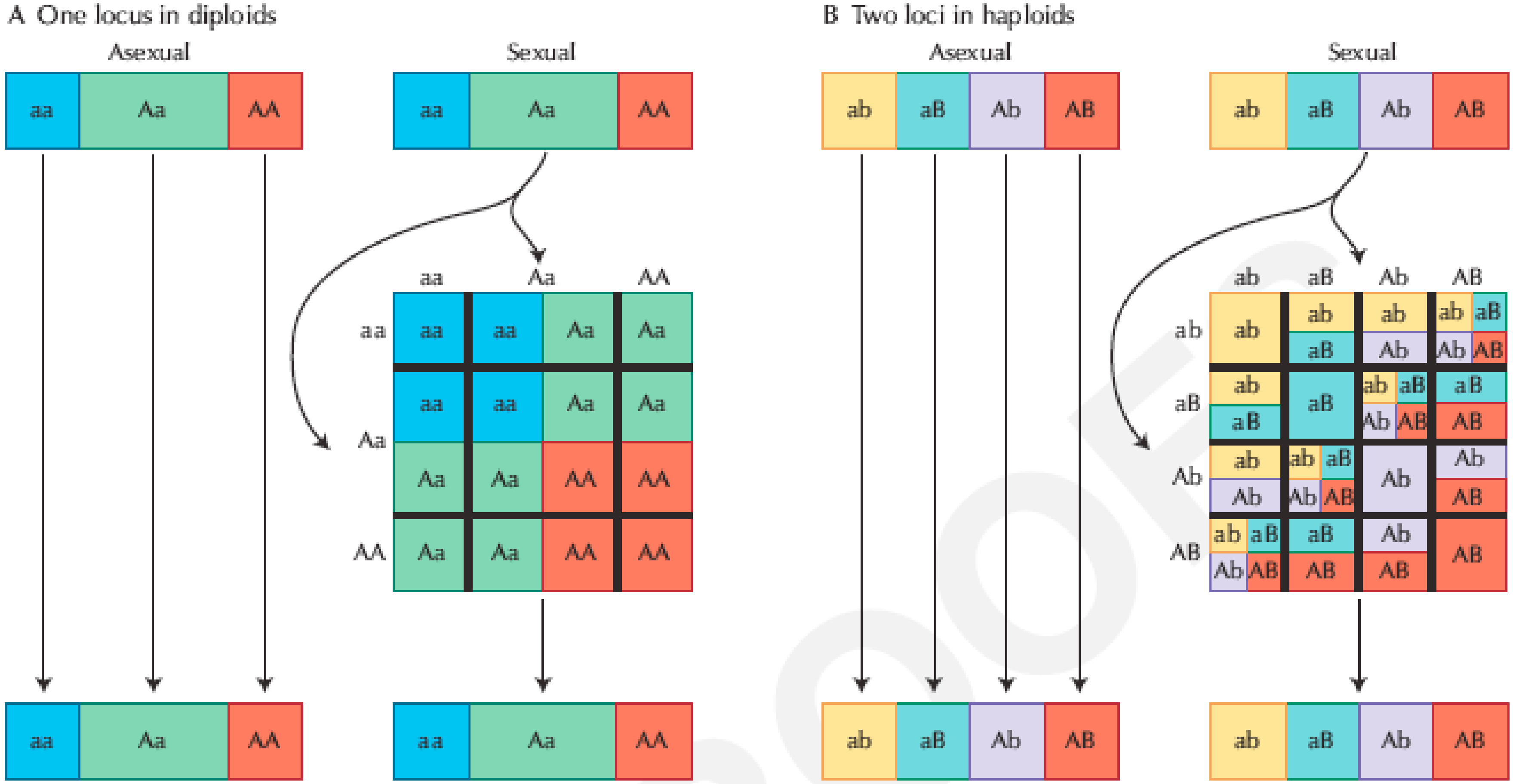

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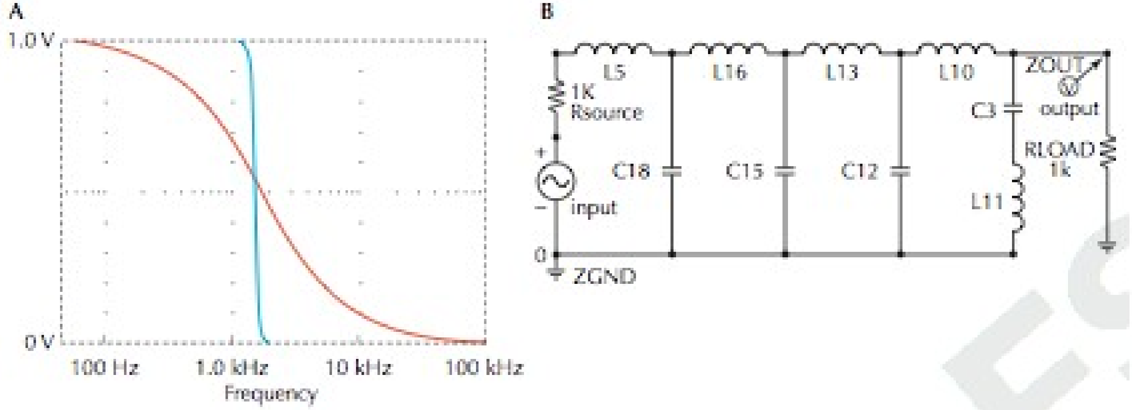

Fisher’s “Fundamental Theorem”:

increase in mean fitness ~ additive variance in fitness

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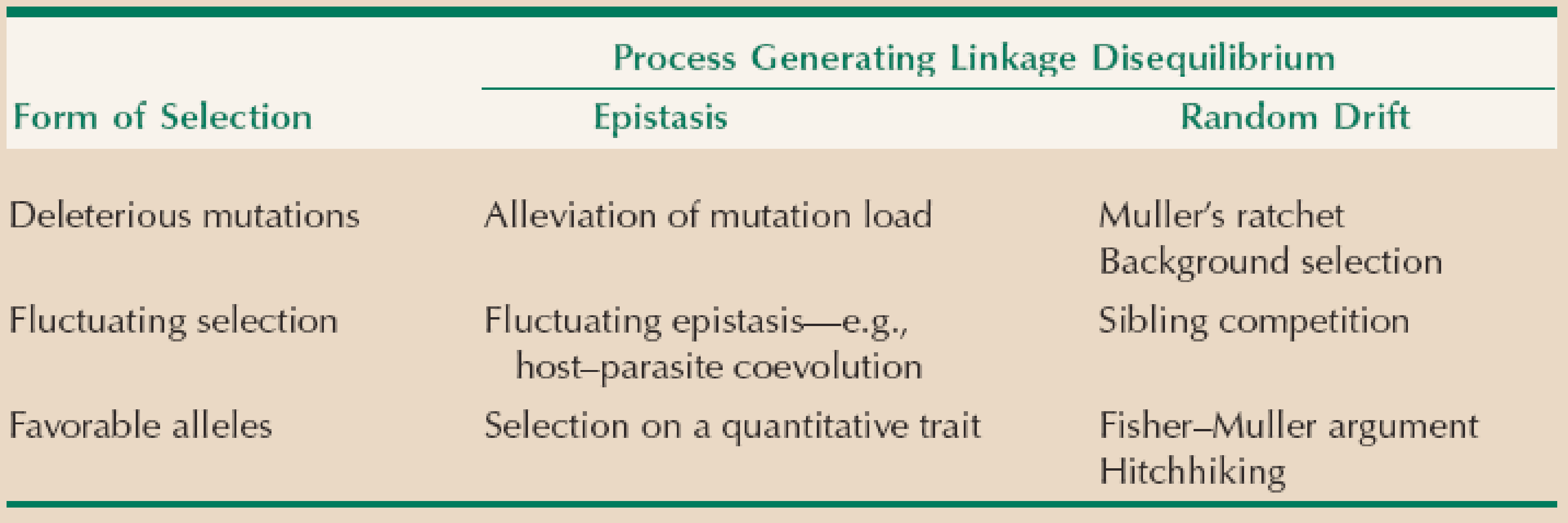
Recombination can only increase V_A if there are negative associations between good alleles

(++--, --++ > ++++, ----)

- Why should there be negative associations?



	Process Generating Linkage Disequilibrium	
Form of Selection	Epistasis	Random Drift
Deleterious mutations	Alleviation of mutation load	Muller's ratchet Background selection
Fluctuating selection	Fluctuating epistasis—e.g., host–parasite coevolution	Sibling competition
Favorable alleles	Selection on a quantitative trait	Fisher–Muller argument Hitchhiking

Felsenstein, *Genetics*, 1974

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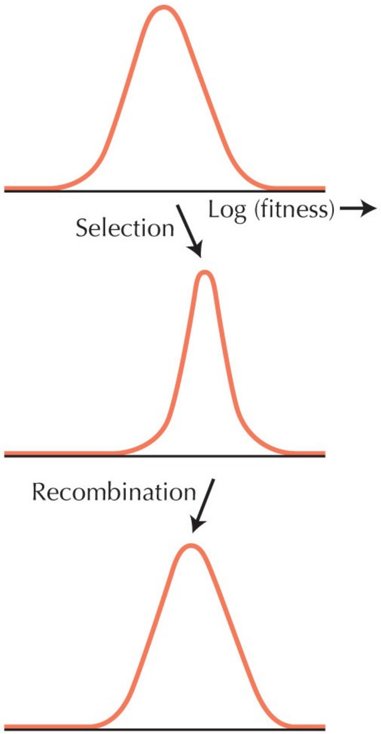


Selection for a recombination modifier:

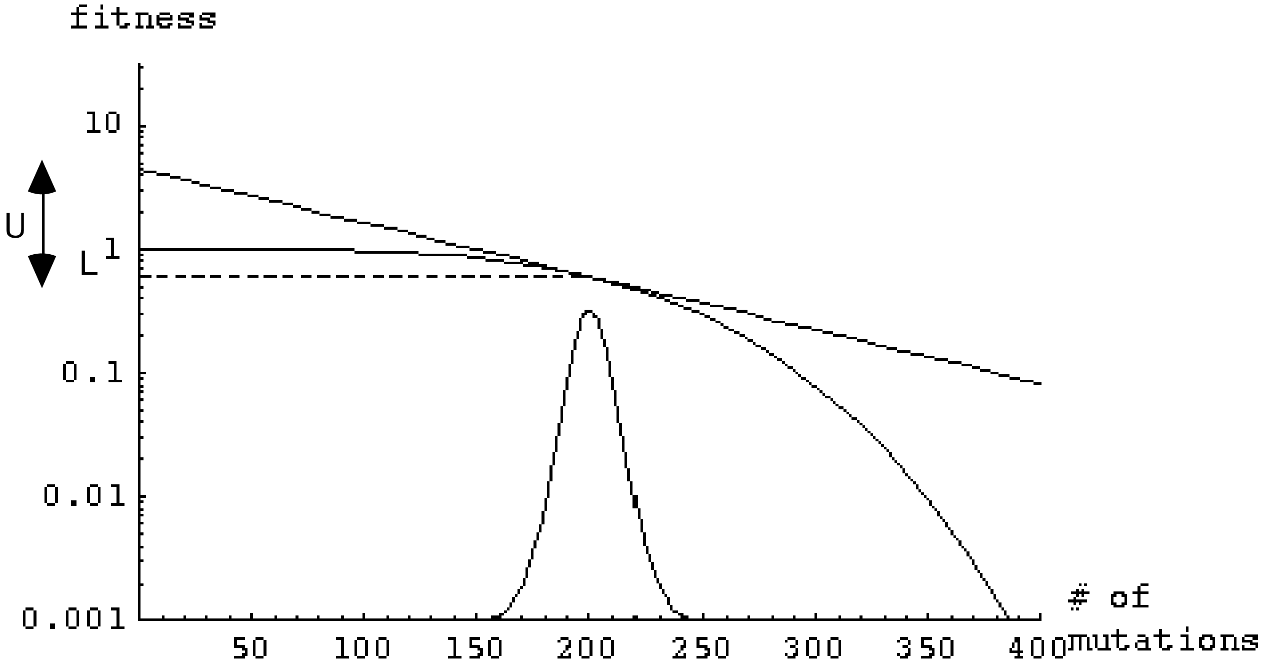
Barton (*Genetical Research* 1995) derived an approximation for the selection favouring a recombination modifier that changes r_{jk} by δr_{jk}:

$$s_{\mathrm{i}} = \frac{\Delta p_{\mathrm{i}}}{p_{\mathrm{i}} q_{\mathrm{i}}} \approx -\frac{v_1}{4} E\left[\frac{\delta r_{\mathrm{jk|i}}}{r_{\mathrm{ijk}}}\left(\frac{1}{r_{\mathrm{ij}}} + \frac{1}{r_{\mathrm{ik}}} - 1\right)\right]$$

$$-\frac{1}{2} \sum_{|N|>1} V'_{|N|} E\left[\frac{\delta r_{N|\mathrm{i}}}{r_N r_{\mathrm{i}N}}\right].$$

Here, v_1 is the component of additive variance in fitness due to LD; If it is –ve, recombination is favoured. $V_{|N|}$ is the non-additive variance due to interactions amongst |N| genes. This is always +ve, and so always selects against recombination

- Negative epistasis:
  - stabilising selection on a quantitative trait
  - reducing the mutation load
    - with no recombination, mutation load is exp(-U)
    - With free recombination, the load is *reduced* if selection is *synergistic*



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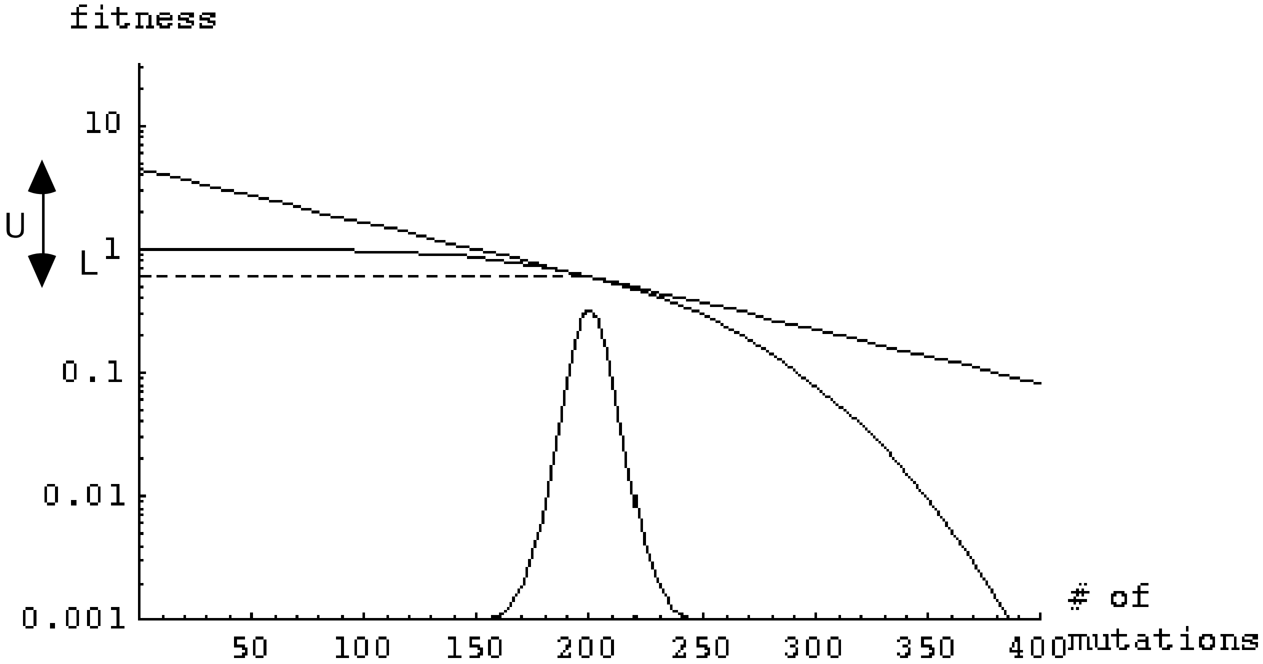

But, are total mutation rates, U, high enough?

Kondrashov, A. S. 1988. Nature 336:435-441.

Stochastic explanations:

- can random drift generate –ve LD ?

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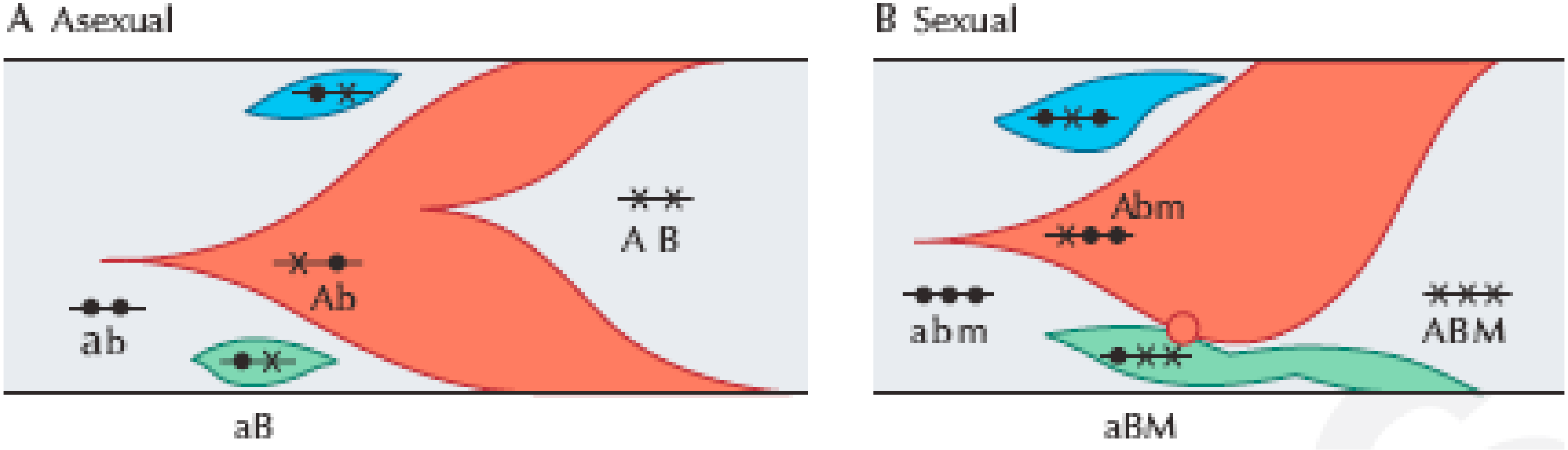
What generates negative associations?

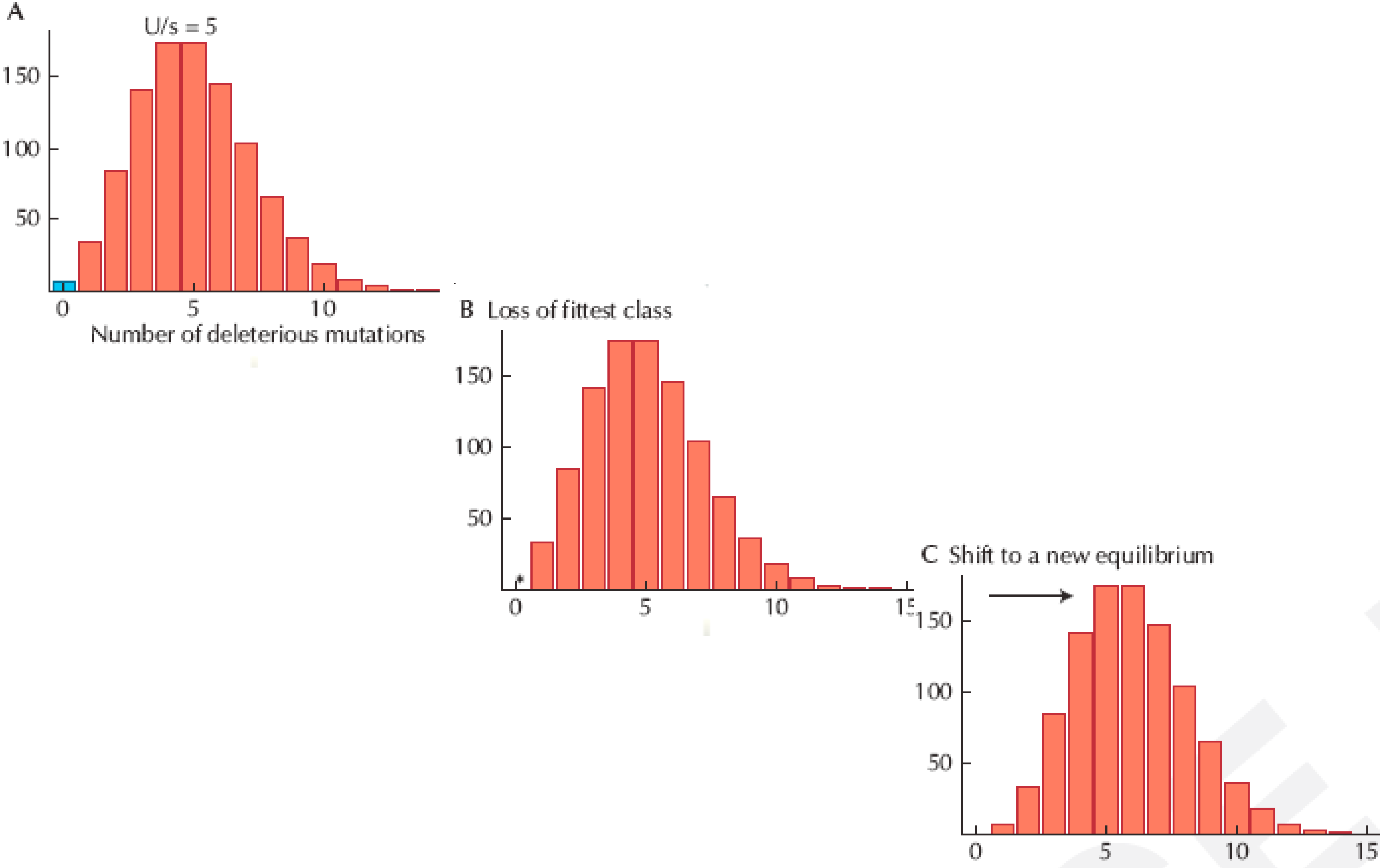
- random drift -> random associations
- selection sweeps out ++, -- leaving +-, -+

In an asexual pop’ln, mutations must fix in series

(Fisher, 1930; Muller, 1932)



- Deleterious mutations accumulate in asexual popl’ns:
  - Muller’s Ratchet



- Hill & Robertson (1966):
    - random drift is due to variation in fitness
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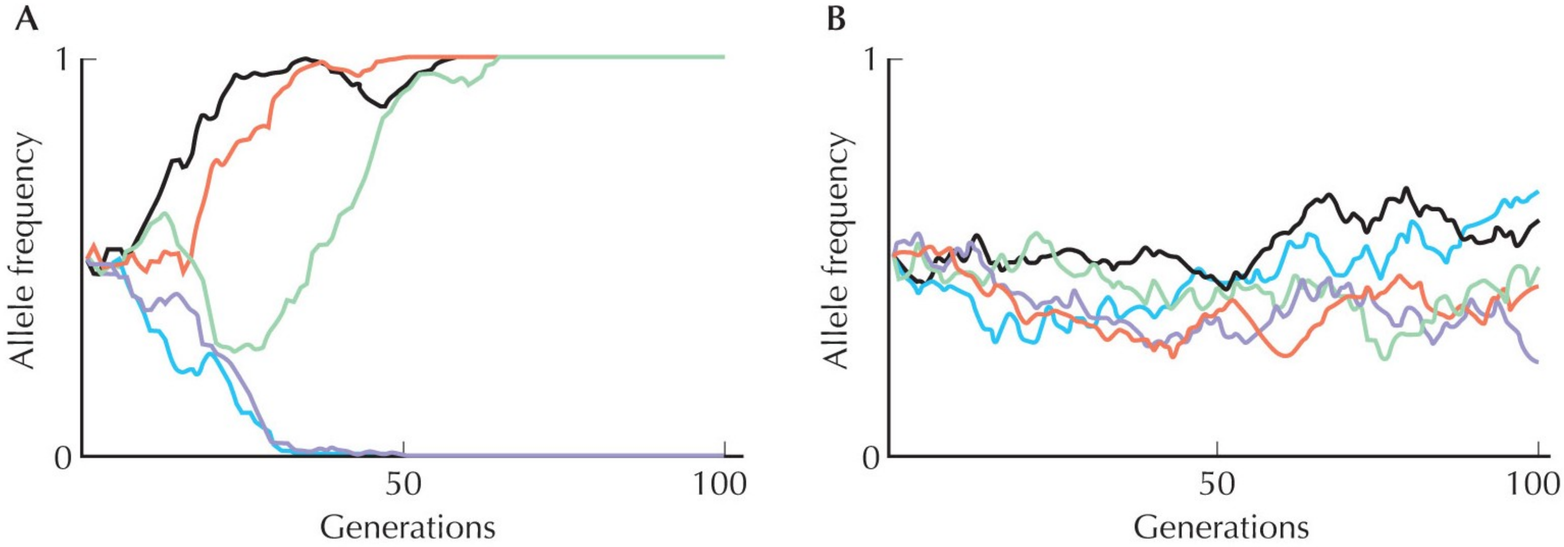

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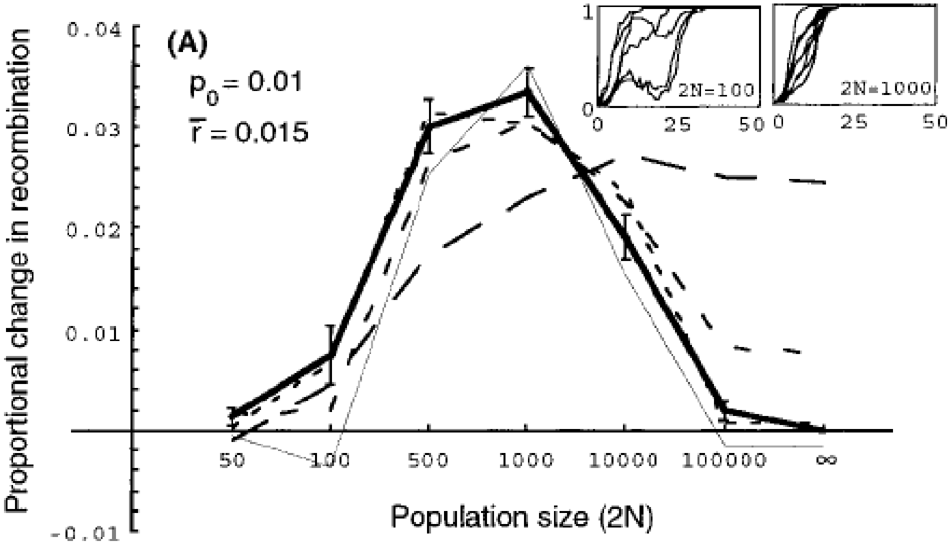
Simulation of two linked loci + modifier:

HR interference can select for recombination
Epistasis is ineffective

(Otto & Barton, *Genetics*, 2001)



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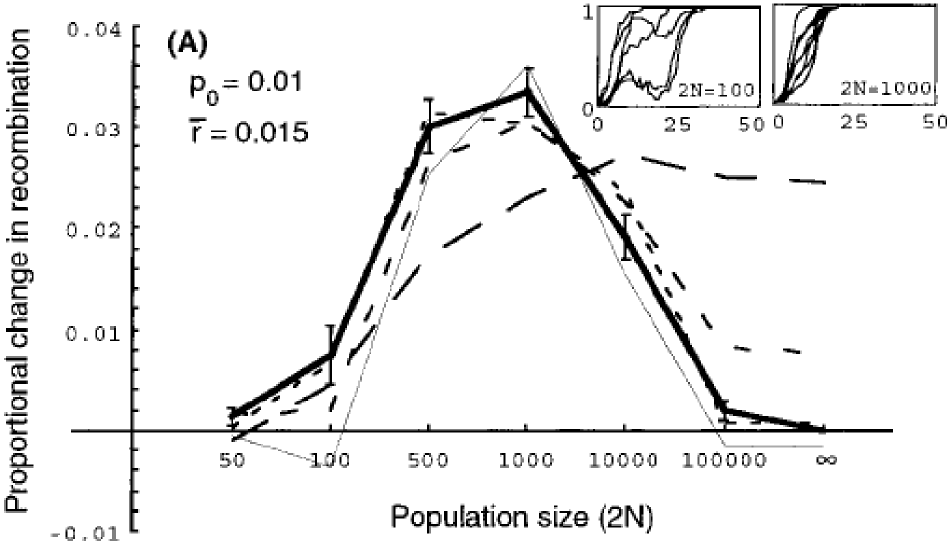
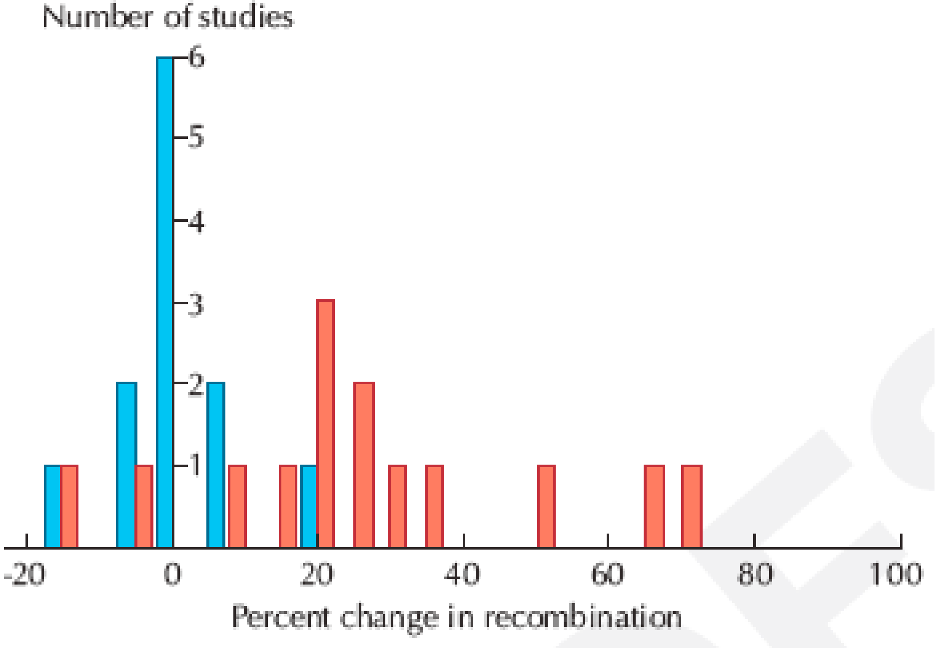


Fixation probability of a favourable allele is reduced to $2\,s\,\frac{N_e}{N}$

Does Hill-Robertson interference impede adaptation?

select for recomb’n?

- Populations under strong selection evolve higher recombination:



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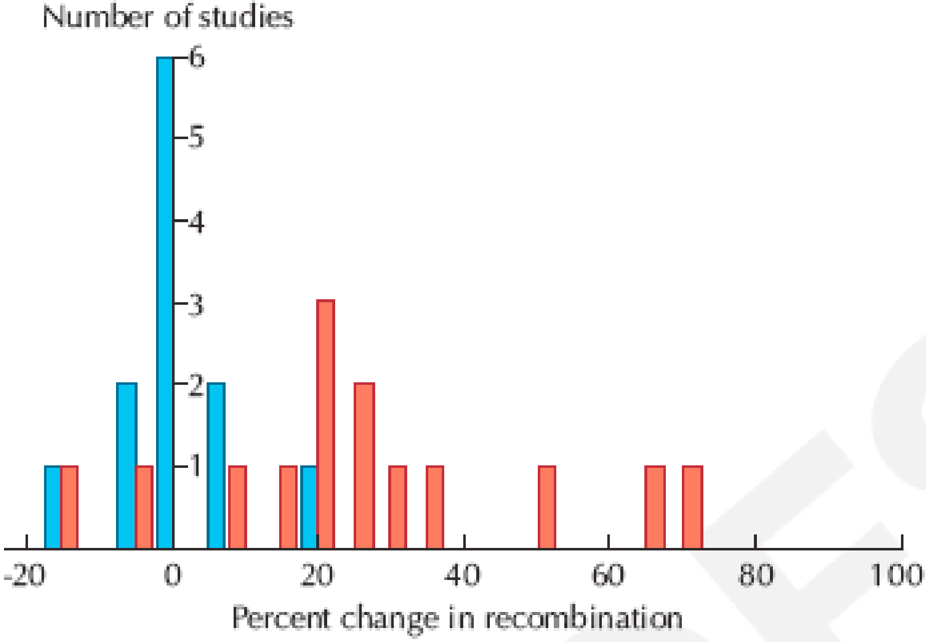
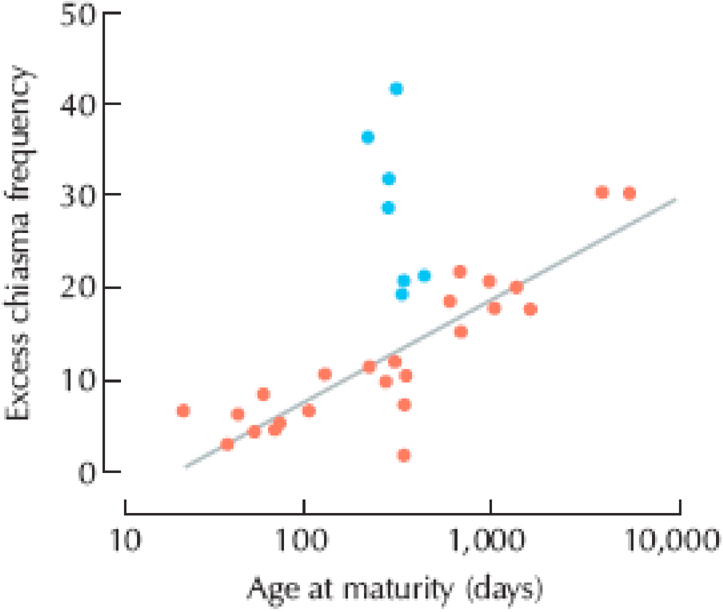
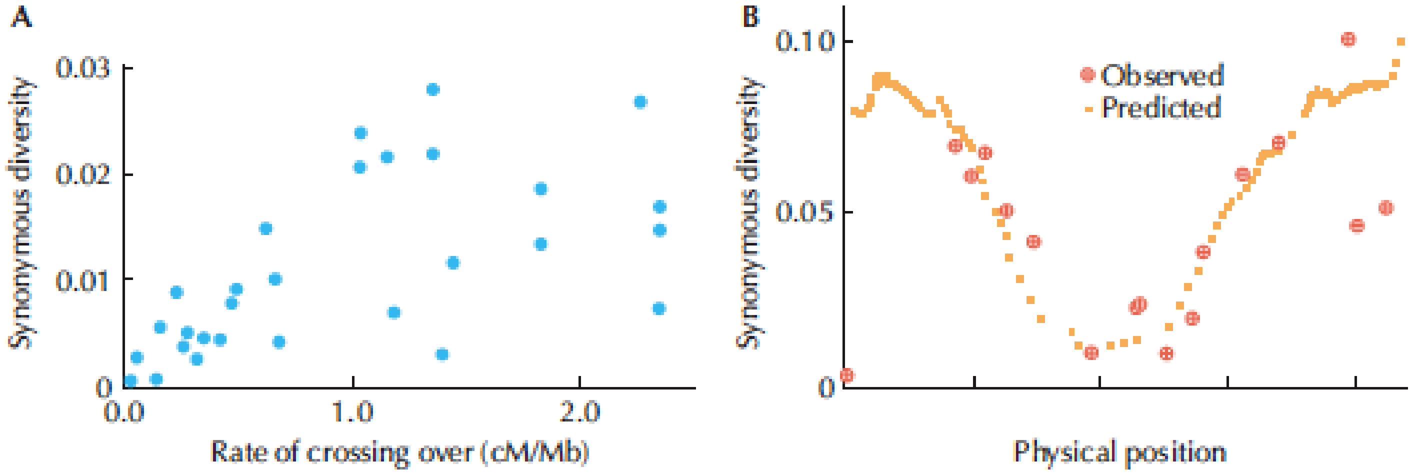


  - Domesticated mammals have more cross-overs



In *Drosophila*, nucleotide diversity is correlated with recombination rate



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e.g. variance in log fitness v = 10%

$0.43<W<1.65$

-> fixation probability reduced by 0.67

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For linked loci, what matters is the rate of adaptive substitution per map length: Λ/R

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**Is there enough heritable variance in fitness to drive selection for recombination ??

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  - Deleterious mutation around ‘wild-type’
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The prevalence of sex implies abundant selection ?