

Fluctuating selection

Why should we be interested?

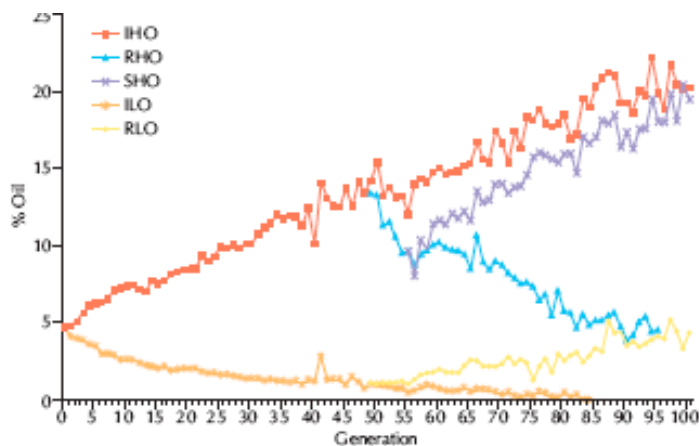
What questions should we answer?

What kind of answers do we look for?

Key observations

■ Selection is effective

- complex adaptations have evolved
 - coded by remarkably little information
- evolution can be rapid
 - human evolution: $\sim 10^5$ years, or 5,000 generations
 - artificial selection (dogs, maize, RNA molecules)



■ Extensive variation

- Rapid, continued response to selection depends on maintenance of heritable variation
- Fitness itself may have high genetic variance
- Extensive molecular diversity across a wide range of organisms

What effect does variation have on fitness?

	genotypic	phenotypic
neutral	✓	×
deleterious	✓	✓
favourable	✓	✓
balancing	✓?	✓?
fluctuating	??	✓??

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Why emphasise fluctuating selection?

- neglected by theory
- If common molecular variants influence fitness, it must be via balancing or fluctuating selection
- Most examples of balancing selection are transient
- Fitness is sensitive to environment

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What constrains the extent of selection?

- # of selected substitutions
 - eg *D. yakuba* and *simulans* diverged ~6Myr ago
 - ~ half of AA substitutions are established by selection (Smith & Eyre-Walker)
 - ~ 300,000 selected AA changes, or ~ 0.03 per year
- genetic variance in fitness is ~1 at most
- genomic mutation rate U is $\ll 1$ for most organisms, but may be ~1 for humans
- sequence diversity ...

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What are the consequences of fluctuating selection?

■ Maintenance of variation

- Fluctuating selection alone cannot maintain variation (Haldane and Jayakar, 1963)
- Spatial heterogeneity can maintain overall variation
 - less effective at maintaining variation within populations

- Mutation and fluctuating selection ?
 - Recurrent sweeps (eg Kondrashov and Yampolsky, 1997)
 - Quantitative trait: Burger (1999), Waxman and Peck (1999)
- Host-parasite coevolution

■ **Interference between selected loci**

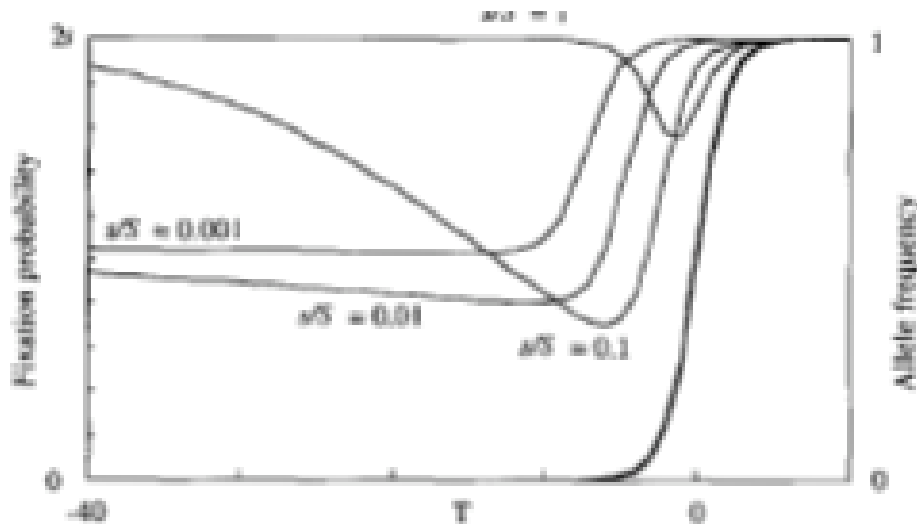
Hill and Robertson (1966) showed that selection at one locus interferes with selection at linked loci

- Favourable alleles compete with eachother
- Random fluctuations interact with selection to generate negative associations ("LD")
- Selection at one locus is perceived as random genetic drift at linked loci

Branching process analysis (Barton, 1995)

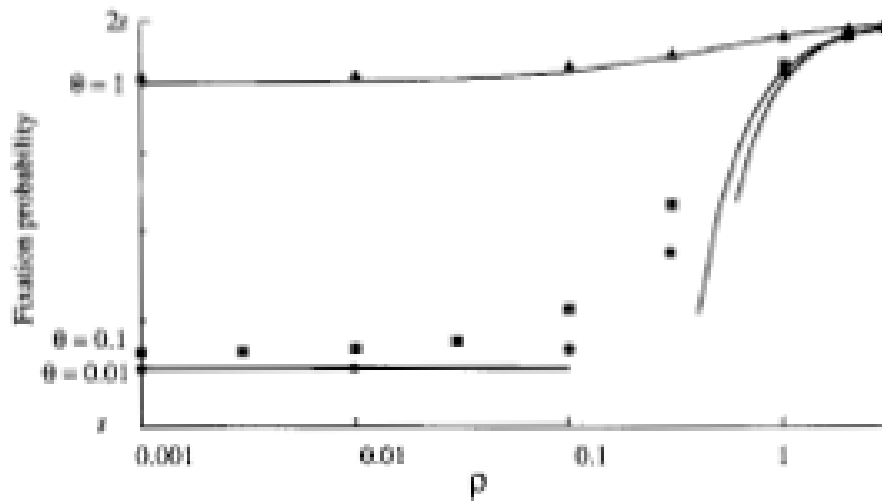
$$\begin{aligned}
 -\frac{\partial P_u}{\partial t} &= -r v (P_u - P_v) + (s + Sv) P_u - \frac{P_u^2}{2} \\
 -\frac{\partial P_v}{\partial t} &= -r u (P_v - P_u) + (s - Su) P_v - \frac{P_v^2}{2}
 \end{aligned}
 \tag{1}$$

e.g. $r = 0.1S$



Fluctuating selection is likely to be the strongest factor causing Hill-Robertson interference:

e.g. alleel frequencies swing between 0.1 and 0.9 at a selected locus:



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Interference with selection at linked loci may be much stronger than effects on neutral diversity

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What kinds of results do we need?

General results that apply for arbitrary $s(t)$

■ Effects on neutral allele frequency

$$\frac{\partial}{\partial t} \text{var} (\Delta u) = \frac{uv}{2N} \left(1 + E \left[\frac{1}{p'q'} \left(\int_{\tau}^{\infty} \frac{\partial p}{\partial \tau} e^{-r(\tau-\tau')} \right)^2 \right] \right) \quad (2)$$

(Barton, 2000, after Maynard Smith & Haigh 1974)

For wild fluctuations, and $r \ll s$:

$$\frac{\partial}{\partial t} \text{var} (\Delta u) = \frac{uv}{2N} \left(1 + \frac{\lambda}{2(2\lambda + r)} E \left[\frac{1}{pq} \right] \right) \quad (3)$$

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■ Effect of selection on genealogies

$$E[\bar{\tau}] = 1 + \text{cov}[\bar{\tau}, W] \quad (4)$$

(Barton & Etheridge, 2004)

Price's equation applies to genealogies...

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General results

Stochastic models

Aggregate effects of multiple loci