Lecture 7. Other types of selection. Mutation-selection balance.

2.6 Other types of selection

Underdominance

Heterozygote inferiority: $w_{AA} > w_{Aa}$ and $w_{aa} > w_{Aa}$

$w_{Aa} = 1$, $w_{AA} = 1 + s_1$, $w_{aa} = 1 + s_2$

$$\boxed{\Delta p = \frac{pq}{\bar{w}}(ps_1 - qs_2),\ \bar{w} = 1 + p^2 s_1 + q^2 s_2}$$

Fig 6.7, p. 235: three equilibria

two locally stable equilibria $\hat{p} = 0$, $\hat{p} = 1$

one unstable equilibrium $\hat{p} = \frac{s_2}{s_1+s_2}$

Ex 11: disruptive selection

North American lacewings (insects): green or brown

two extreme colors provide camouflage in two different niches, but intermediate color offers no protection

This type of selection maintains population diversity

it might even cause one species to evolve into two

Frequency-dependent selection

Genotype fitness decreases with its frequency

$w_{AA} = 1 - c \cdot p^2$, $w_{Aa} = 1 - 2c \cdot p \cdot q$, $w_{aa} = 1 - c \cdot q^2$

c is a positive constant of proportionality

$$\boxed{\Delta p = \frac{c}{\bar{w}} pq(q - p)(p^2 - pq + q^2)}$$

Stable equilibrium $\hat{p} = \hat{q} = 0.5$

despite heterozygote inferiority in the equilibrium state

$w_{AA} = w_{aa} = 1 - \frac{c}{4}$, $w_{Aa} = 1 - \frac{c}{2}$

2.7 Mutation-selection balance

Directional selection favoring allele A

increases p $\quad \Delta p = spq[ph + q(1 - h)]$

Irreversible harmful recurrent mutation of rate μ

decreases p $\quad \Delta p = -p\mu$

Combined effect $\quad \Delta p = spq[ph + q(1 - h)] - p\mu$

$$\boxed{\text{Equilibrium equation:}\quad pqh + q^2(1 - h) = \frac{\mu}{s}}$$

Equlibrium frequencies of the harmful allele

$$\boxed{\hat{q} = \sqrt{\frac{\mu}{s}},\ \text{if } h = 0} \qquad \boxed{\hat{q} = \frac{\mu}{hs},\ \text{if } 0 < h \le 1,\ p \approx 1}$$

Typically $\mu = 10^{-5}$ to 10^{-6} while $s = 10^{-1}$ to 10^{-2}

$h = 1$ (dominant disease): $\hat{q} = 10^{-3}$ to 10^{-5}

$h = 0$ (recessive disease): $\hat{q} = 3 \cdot 10^{-2}$ to $3 \cdot 10^{-3}$

Fig 6.8, p. 238: let $\mu = 5 \cdot 10^{-6}$ and $s = 1$

$\hat{q} = \sqrt{\mu} = 0.0022$ if $h = 0$ compare with

$\hat{q} = \frac{\mu}{h} = 0.0002$ if $h = 0.025$

Ex 13: cystic fibrosis

Two possible explanations of the polymorphism $\hat{q} = 0.02$

mutation-selection balance $w_{AA} = w_{Aa} = 1$, $w_{aa} = 0$

overdominance $w_{AA} < w_{Aa} = 1$, $w_{aa} = 0$

Mutation-selection balance $s = 1$, $h = 0$

$\mu = \hat{q}^2 = 0.0004$ unrealistically high mutation rate

Overdominance $\hat{q} = \frac{s_1}{1+s_1}$, $s_1 = 0.02$

heterozygotes are resistant against typhoid fever

2% advantage in heterozygous fitness

Mutation load

Mutation load = reduction in average fitness

caused by recurrent harmful mutation

Mutation load $L = 1 - \bar{w}$ for $0 \leq h \leq 1$, $s > 0$

Haldane-Muller principle

1. if $h = 0$, then $L = \mu$ is independent of s
2. if $h > 0$, then $L = 2\mu$ is independent of s and h

The effect of deleterious mutation on the mean

population fitness depends only on mutation rate

and not on severity of mutations

Milder mutations are present at higher frequency

whereas more severe mutations have lower frequency

Segregation distortion

Non-Mendelian segregation

heterozygotes Aa produce a skewed ratio $k : (1-k)$

of A-gametes and a-gametes

Segregation distortion without selection

leads to fixation of allele A if $k > 0.5$

Assuming random mating

$p_t = p_{t-1}^2 + k2p_{t-1}q_{t-1}$, $q_t = q_{t-1}^2 + (1-k)2p_{t-1}q_{t-1}$

$\Delta p = pq(2k-1)$ like add. selection with $\frac{s}{2} = 2k - 1$

Literature:

1. D.L.Hartl, A.G.Clarc. Principle of population genetics. Sinauer Associates, 2007.
2. R.Nielson, M. Statkin. An introduction to population genetics: theory and applications, Sinauer Associates. 2013.