Evolutionary safety of lethal mutagenesis –S2 Text File: Step-by-step derivation of Eq. 22

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$$V = \frac{(a_1 - a_0)e^{(bq^m - a_0)T}}{(bq^m - a_0)(a_1 - bq^m)}$$

$$X = \frac{(a_1 - a_0)e^{(bq^{m+n} - a_0)T}}{(bq^{m+n} - a_0)(a_1 - bq^{m+n})}$$

$$Y = V - X$$

Let us introduce the function:

$$F(x) = \frac{e^{bTq^x}}{(q^x - g_0)(g_1 - q^x)} \tag{1}$$

Here $g_i = a_i/b$. Notice that $g_0 < 1 < g_1$. We have

$$V = F(m)\,(g_1 - g_0)\,e^{-a_0T}$$

$$X = F(m+n)\,(g_1 - g_0)\,e^{-a_0T}$$

$$Y = [F(m) - F(m+n)](g_1 - g_0)\,e^{-a_0T}$$

Approximating $q^x = (1-u)^x \approx 1 - ux$ we get

$$F(x) = \frac{e^{bT(1-ux)}}{(1 - ux - g_0)(g_1 - 1 + ux)} \tag{2}$$

Let $f_0 = 1 - g_0 > 0$ and $f_1 = g_1 - 1 > 0$. We get

$$F(x) = \frac{e^{bT(1-ux)}}{(f_0 - ux)(f_1 + ux)} \tag{3}$$

For $ux \ll 1$ we get

$$F(x) = \frac{e^{-bTux}e^{bT}}{f_0f_1 + ux(f_0 - f_1)} \tag{4}$$

Let $h = bT$ and $k = (f_0 - f_1)/(f_0f_1)$.

$$F(x) = \frac{e^{-hux}}{1 + kux}\frac{e^h}{f_0f_1} \tag{5}$$

The derivative of $F(m) - F(m+1)$ with respect to u is $[G(m+1) - G(m)]e^{h}/(f_0 f_1)$ where

$$G(x) = \frac{x(h+k+hkxu)e^{-hxu}}{(1+kxu)^2}$$

The optimum of u is found by solving $G(m) = G(m+1)$ for u. We have

$$\frac{m(h+k+hkmu)e^{-hmu}}{(1+kmu)^2} = \frac{(m+1)(h+k+hk(m+1)u)e^{-h(m+1)u}}{(1+k(m+1)u)^2}$$

Canceling e^{-hmu} we get

$$\frac{m(h+k+hkmu)}{(1+kmu)^2} = \frac{(m+1)(h+k+hk(m+1)u)e^{-hu}}{(1+k(m+1)u)^2}$$

Approximating $e^{-hu} \approx 1 - hu$ we get

$$\frac{m(h+k+hkmu)}{(1+kmu)^2} = \frac{(m+1)(h+k+hk(m+1)u)(1-hu)}{(1+k(m+1)u)^2}$$

Rearranging we get

$$\left(\frac{1+kmu+ku}{1+kmu}\right)^2 = \left(1+\frac{1}{m}\right)(1-hu)\frac{h+k+hkmu+hku}{h+k+hkmu}$$

Which is

$$\left(1+\frac{ku}{1+kmu}\right)^2 = \left(1+\frac{1}{m}\right)(1-hu)\frac{h+k+hkmu+hku}{h+k+hkmu}$$

Assuming $\left(1+\frac{ku}{1+kmu}\right)^2 \approx 1+\frac{2ku}{1+kmu}$ we get

$$1+\frac{2ku}{1+kmu} = \left(1+\frac{1}{m}\right)(1-hu)(1+\frac{hku}{h+k+hkmu})$$

Multiplying on the RHS and neglecting higher terms we get

$$\frac{2ku}{1+kmu} = \frac{1}{m} - hu + \frac{hku}{h+k+hkmu}$$

Multiplying with m we get

$$\frac{2kmu}{1+kmu} = 1 - hmu + \frac{hkmu}{h+k+hkmu}$$

Rearranging we get

$$hmu + \frac{2kmu}{1+kmu} - \frac{hkmu}{h+k+hkmu} = 1$$

Let $x = mu$

$$hx + \frac{2kx}{1 + kx} - \frac{hkx}{h + k + hkx} = 1$$

Which is equivalent to

$$h + k + x(h^2 + k^2) + x^2hk(2h + k) + x^3h^2k^2 = 0$$