FILE S2

INCORPORATING BACK MUTATIONS

In our derivation of the time-dependent effective population size, we have neglected the effect of back mutations. In practice, back mutations only introduce terms of higher-order in μ/s, and thus are of negligible contribution in the regime we consider. However, it is straightforward to incorporate these terms into our analysis, which we do here.

First, we consider the steady-state distribution of mutations at a single site. This is determined by the solution to the equations:

$$\begin{aligned} f_1 &= \frac{f_1(1-s)}{\overline{\omega}}(1-\mu_b) + \frac{f_0}{\overline{\omega}}\mu_f \\ f_0 &= \frac{f_1(1-s)}{\overline{\omega}}\mu_b + \frac{f_0}{\overline{\omega}}(1-\mu_f), \end{aligned}$$

where μ_f and μ_b are the forward and back mutation rates, respectively. This yields:

$$\begin{aligned} f_1 &= \frac{s+\mu_b(1-s)+\mu_f-\sqrt{(s+\mu_b(1-s)+\mu_f)^2-4s\mu_f}}{2s} \\ f_0 &= \frac{s-\mu_b(1-s)-\mu_f+\sqrt{(s+\mu_b(1-s)+\mu_f)^2-4s\mu_f}}{2s}. \end{aligned}$$

When $\mu_b = 0$, these reduce to the usual mutation-selection balance results, $f_1 = \mu_f/s$ and $f_0 = 1-\mu_f/s$. Furthermore, if we define $\mu_f \equiv \mu$ and $\mu_b \equiv c\mu$, and expand this result in orders of μ/s, we see that:

$$\begin{aligned} f_1 &= \frac{\mu}{s} - \frac{\mu^2}{s^2}c(1-s) + \frac{\mu^3}{s^3}(c^2(1-s)^2 - c(1-s))\ldots \\ f_0 &= 1 - \frac{\mu}{s} + \frac{\mu^2}{s^2}c(1-s) - \frac{\mu^3}{s^3}(c^2(1-s)^2 - c(1-s))\ldots \end{aligned}$$

Thus, we see that incorporating back mutations leads to a correction of order μ^2/s^2. As a consequence, the effect of back mutations is negligible in the regime we consider. However, we may derive Equation 2 from the main text including them. We have that:

$$\frac{dP_{mut}(t)}{dt} = -\left(rx + \frac{\mu_f N f_0}{N f_1} + \frac{\mu_b N f_1}{N f_0}\right)P_{mut}(t) + rxf_1 + \frac{\mu_b N f_1}{N f_0}$$

Solving this yields:

$$P_{mut}(x,t) = \frac{rxf_1 + \frac{\mu_b f_1}{f_0}}{rx + \frac{\mu_f f_0}{f_1} + \frac{\mu_b f_1}{f_0}} + \frac{\mu_f f_0 - \mu_b f_1}{rx + \frac{\mu_f f_0}{f_1} + \frac{\mu_b f_1}{f_0}} e^{-\left(rx + \frac{\mu_f f_0}{f_1} + \frac{\mu_b f_1}{f_0}\right)t}.$$

which replaces Equation 2 in the main text. Similarly, Equation 1 may be recovered by substituting $rx \to r(x_i, x_f)$. We note that these equations are identical to those given in the main text to leading-order in μ/s, and thus back mutations represent only a small correction to our results in the regime we consider.