Supplementary Note

A derivation of the probability of fixation using Wahl, Gerrish and Saika-Voivod (2002) model for arbitrary selection coefficients

The mathematical derivations below are based on Wahl and Gerrish (2001) and Wahl, Gerrish and Saika-Voivod (2002). Both papers consider a mathematical model for experimental evolution and both assume that exponential growth occurs during each cycle followed by a flask transfer which produces a bottleneck that reduces the population to its original size. Using the notation in Wahl and Gerrish (2001), we define r as the growth rate, D as the dilution factor, and s as the selection coefficient of the newly arisen mutant and τ as the length of time of each cycle. It is assumed that the mutant with selective advantage s arises at sometime t during a particular cycle. To calculate the probability that the mutant eventually fixes in the population $\Pi(s,t)$ we first calculate the probability that the mutant is lost due to the effects of the bottleneck. We denote this probability by $V(s,t)$. Wahl and Gerrish (2001) showed that the solution to $V(s,t)$ results from solving the following two equations. First we must solve for y below

$$1 - y = e^{-Dye^{r(1+s)\tau}}. \tag{1}$$

We then take the solution to (1) and place into (2) below

$$V(s,t) = e^{-Dye^{r(1+s)(\tau-t)}} \tag{2}$$

where t is the time the mutant with selection coefficient s arises. To calculate the relevant probability that a mutant fixes we simply note that $\Pi(s,t) = 1 - V(s,t)$. Equation (1) represents the probability that a mutant which arose during a cycle and made it through that bottleneck will fix and $V(s,t)$ is the probability that a mutant that arises during a cycle at time t will eventually go extinct. For many applications of interest $y \approx 1$ and $V(s,t) \approx e^{-De^{r(1+s)(\tau-t)}}$ which is the probability of not making it through the first bottleneck.

In Wahl, Gerrish and Saika-Voivod (2002) equation (2) is extended to consider the fact that the time at which a mutant arises is random with probability proportional to the number of individuals. Therefore, it is more common for a mutant to arise during the end of a cycle, but mutants that arise during the end of a cycle will have a smaller chance of passing through the bottleneck. However, Wahl, Gerrish and Saika-Voivod (2002) stop short of deriving the probability of fixation except in the case where s is small. A third paper by Heffernan and Wahl (2002) does derive a large s version of the probability of fixation but for a more general model. For this reason we derive the formula for the probability of fixation without making the small s assumption, but maintain the simplicity of the original Wahl *et.al.*(2002) model.

Let t be distributed as follows

$$f(t) = \frac{re^{rt}}{e^{r\tau} - 1} \quad 0 \le t \le \tau.$$

Then if we average over t we get

$$V(s) = \frac{\int_0^\tau e^{-Dye^{r(1+s)(\tau-t)}} re^{rt}}{e^{r\tau} - 1} dt.$$

The above integral can be solved by a series of substitutions and integration by parts. To this end let

$$\begin{aligned}
&x = e^{-r(1+s)t} \\
&dx = -r(1+s)e^{-r(1+s)t} = -r(1+s)xdt \\
&\frac{1}{x^{1/(1+s)}} = e^{rt}.
\end{aligned}$$

Define $\alpha = Dye^{r(1+s)\tau}$. Therefore

$$\begin{aligned}
V(s) &= \frac{\int_0^\tau e^{-De^{r(1+s)(\tau-t)}} re^{rt}}{e^{r\tau}-1} dt \\
&= \frac{r}{e^{r\tau}-1} \int_1^{e^{-r(1+s)\tau}} \frac{e^{-\alpha x}}{-r(1+s)xx^{1/(1+s)}} dx \\
&= \frac{1}{(1+s)(e^{r\tau}-1)} \int_{e^{-r(1+s)\tau}}^1 \frac{e^{-\alpha x}}{x^{1+1/(1+s)}} dx \\
&= \frac{1}{(1+s)(e^{r\tau}-1)} \int_{e^{-r(1+s)\tau}}^1 e^{-\alpha x} x^{-1-1/(1+s)} dx.
\end{aligned} \tag{3}$$

Now consider integration by parts to get

$$\begin{aligned}
u &= e^{-\alpha x} & dv &= x^{-\frac{1}{1+s}-1}dx \\
du &= \alpha e^{-\alpha x}dx & v &= -(1+s)x^{\frac{-1}{1+s}}.
\end{aligned}$$

Substituting $\int udv = uv - vdu$ above and noting that $(Dy/\alpha)^{\frac{-1}{1+s}} = e^{r\tau}$ we get

$$\int_{Dy/\alpha}^1 e^{-\alpha x}x^{-1-1/(1+s)}dx = (s+1)e^{-Dy}e^{r\tau} - (s+1)e^{-\alpha} - \alpha(s+1)\int_{Dy/\alpha}^1 e^{-\alpha x}x^{-\frac{1}{s+1}}dx. \tag{4}$$

A second application of integration by parts to the remaining integral above gives

$$\int_{Dy/\alpha}^1 e^{-\alpha x}x^{-\frac{1}{s+1}}dx = \frac{s+1}{s}e^{-\alpha} - \frac{s+1}{s}e^{-rs\tau}e^{-Dy} + \frac{s+1}{s}\alpha\int_{Dy/\alpha}^1 e^{-\alpha x}x^{\frac{s}{s+1}}dx. \tag{5}$$

Note that $e^{r\tau}-1 \approx e^{r\tau}$ and this is approximation will make the remaining formulas more manageable. Appropriately substitution equations (4)and (5) into (3) gives

$$\begin{aligned}
\frac{1}{(1+s)e^{r\tau}}\int_{e^{-r(1+s)\tau}}^1 e^{-\alpha x}x^{-1-1/(1+s)}dx &= e^{-Dy} - e^{-\alpha-r\tau} - \alpha\tfrac{s+1}{s}e^{-\alpha-r\tau} + \tfrac{s+1}{s}\alpha e^{-rs\tau}e^{-r\tau}\alpha e^{-Dy} \\
&\quad - \frac{\alpha^2(s+1)}{se^{r\tau}}\int_{Dy/\alpha}^1 e^{-\alpha x}x^{\frac{s}{s+1}}dx \\
&= e^{-Dy} - e^{-\alpha-r\tau} - \alpha\tfrac{s+1}{s}e^{-\alpha-r\tau} + \tfrac{s+1}{s}Dye^{-Dy} \\
&\quad - (Dy)^{\frac{1}{s+1}}\,\tfrac{s+1}{s}\Gamma\left(\tfrac{s}{s+1}+1\right)\int_{Dy/\alpha}^1 \frac{\alpha(\alpha x)^{s/(s+1)}e^{-\alpha x}}{\Gamma\left(\frac{s}{s+1}+1\right)}dx.
\end{aligned}$$

The last equation follows by noting that $\alpha^2 = \alpha \cdot \alpha^{s/(s+1)}\alpha^{1/(s+1)}$ and that $\alpha^{1/(s+1)} = (Dy)^{1/(s+1)} e^{r\tau}$ Note further that $\frac{s+1}{s}\Gamma\left(\frac{s}{s+1}+1\right) = \Gamma\left(\frac{s}{s+1}\right)$. Now let Y be a Gamma distributed random variable with shape parameter $\frac{s}{s+1}+1$ and scale parameter α, that is $Y \sim$GAM$\left(\alpha, \frac{s}{s+1}+1\right)$. Then

$$\begin{aligned}
V(s) \;&= e^{-Dy} - e^{-\alpha-r\tau} - \alpha\tfrac{s+1}{s}e^{-\alpha-r\tau} + \tfrac{s+1}{s}Dye^{-Dy} \\
&- (Dy)^{\frac{1}{s+1}}\,\Gamma\left(\tfrac{s}{s+1}\right)P\left(\tfrac{Dy}{\alpha} \le Y \le 1\right) \\
&= e^{-Dy}\left[1+\tfrac{s+1}{s}Dy\right] - e^{-\alpha-r\tau}\left[1+\alpha\tfrac{s+1}{s}\right] - (Dy)^{\frac{1}{s+1}}\,\Gamma\left(\tfrac{s}{s+1}\right)P\left(\tfrac{Dy}{\alpha} \le Y \le 1\right).
\end{aligned}$$

Therefore the probability of fixation $\Pi(s) = 1 - V(s)$ is given by first solving y

$$1 - y = e^{-Dye^{r(1+s)\tau}} \tag{6}$$

and then substitute y into

$$\begin{aligned}
\Pi(s) \;&= (Dy)^{\frac{1}{s+1}}\,\Gamma\left(\tfrac{s}{s+1}\right)P\left(\tfrac{Dy}{\alpha} \le Y \le 1\right) \\
&+ e^{-\alpha-r\tau}\left[1+\alpha\tfrac{s+1}{s}\right] + 1 - e^{-Dy}\left[1+\tfrac{s+1}{s}Dy\right].
\end{aligned} \tag{7}$$

where $\alpha = Dye^{r(1+s)\tau}$.

For $s > .3$ then $y \approx 1$. In general the solution to equation (6) is solved by a series of iterations. Begin with an initial $y_0 = 1$ and substitute this into the right hand side of equation (6) to obtain $y_1 = 1 - e^{-De^{r(1+s)\tau}}$. In general $y_{n+1} = 1 - e^{-Dy_n e^{r(1+s)\tau}}$. Typically, convergence is quite fast and one can stop after 2 or 3 iterations.

Heffernan, J.M. & Wahl, L.M. The effects of genetic drift in experimental evolution. *Theo Pop Bio* **62**, 349-356, (2002).

Wahl, L.M., Gerrish, P.J. & Saika-Voivod, I. Evaluating the impact of population bottlenecks in experimental evolution. *Genetics* **162** , 961-971 (2002).

Wahl, L.M. & Gerrish, P.J. The probability that beneficial mutations are lost in populations with periodic bottlenecks. *Evolution* **55**, 2606-2610 (2001).