

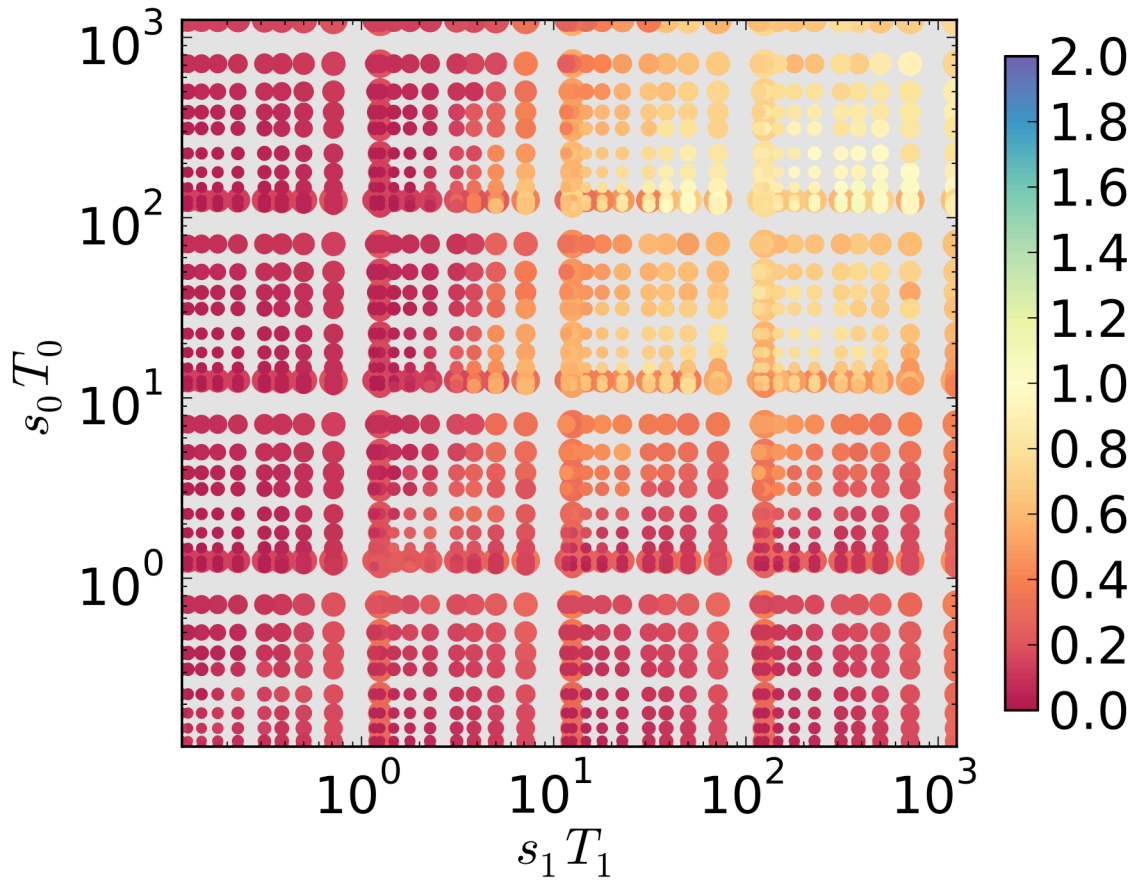
Supplementary material for “Broad Conditions Favor the Evolution of Phase-Variable Loci”

M.E. Palmer, M. Lipsitch, E.R. Moxon, and C.D. Bayliss

Geometrically distributed epoch lengths

In the figures in the main text of the article, the E_0 and E_1 epochs had constant lengths of T_0 , and T_1 , respectively. In bacterial populations in the wild, we cannot expect strictly constant epoch lengths to be common. We might instead expect an exponential distribution of epoch lengths, assuming, for instance, a certain average probability that a bacterium will be transmitted from one host to the next, per unit time.

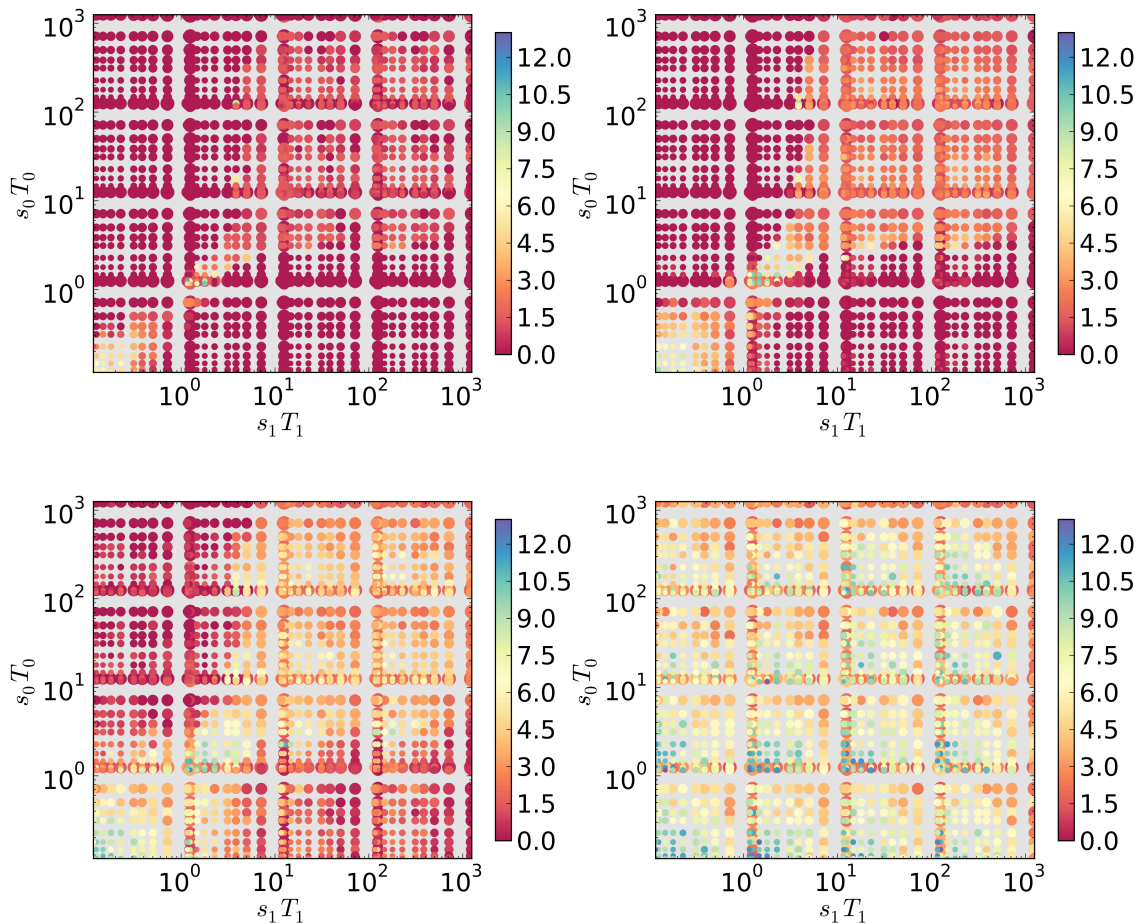
To investigate the effect of geometrically distributed epoch lengths, we ran the same experiments that were plotted in Figure 5 of the main text, but made the durations of the individual E_0 epochs geometrically distributed with mean length T_0 , and the durations of the individual E_1 epochs geometrically distributed with mean length T_1 . The results are plotted in Supplementary Figure 1. In this case, any particular replicate run with certain values of T_0 and T_1 will experience a variety of epoch lengths (of mean T_0 in the E_0 epochs, and mean T_1 in the E_1 epochs) over time. The exponential distribution produces many epochs that are of shorter length than the mean, and a few epochs that are much longer than the mean. Thus, even when $sT \geq 7$ (with T indicating the mean length of geometrically distributed epoch lengths), many individual epochs will fall below the required sT threshold, which favors a minimal mutation rate. The result, shown in Supplementary Figure 1, is that evolved mutation rates are depressed (orange values, rather than yellow), compared to Figure 5 of the main text, especially for lower values of sT . However, as the sT increases past 7 in both environments, more and more individual epochs begin to favor a non-minimal mutation rate. Thus, although there is not such a sharp transition between evolved minimal and non-minimal mutation rates, the same sT threshold determines whether an *individual* epoch will favor a minimal, or a non-minimal, rate. The low-but-symmetrical sT case in which non-minimal mutation rate is produced is still present, but is also “blurred” due to the fact that a single T_0 or T_1 value represents a distribution of epoch lengths about a mean, rather than a single fixed epoch length.



Supplementary Figure 1: Geometrically distributed epoch lengths. T_0 is the mean length of the E_0 epochs, and T_1 is the mean length of the E_1 epochs. The ratio μ_{win}/μ_{avg} is indicated by the color of the circles. Although the exponential distribution produces many epochs shorter than the mean length (and a small number of much longer ones), the threshold of $s_0 T_0 > 7$ and $s_1 T_1 > 7$, required to favor a non-minimal mutation rate (i.e., points of other than dark red color) still applies. $N=10^9$.

When the population size becomes low, the standard deviation in winning length becomes large

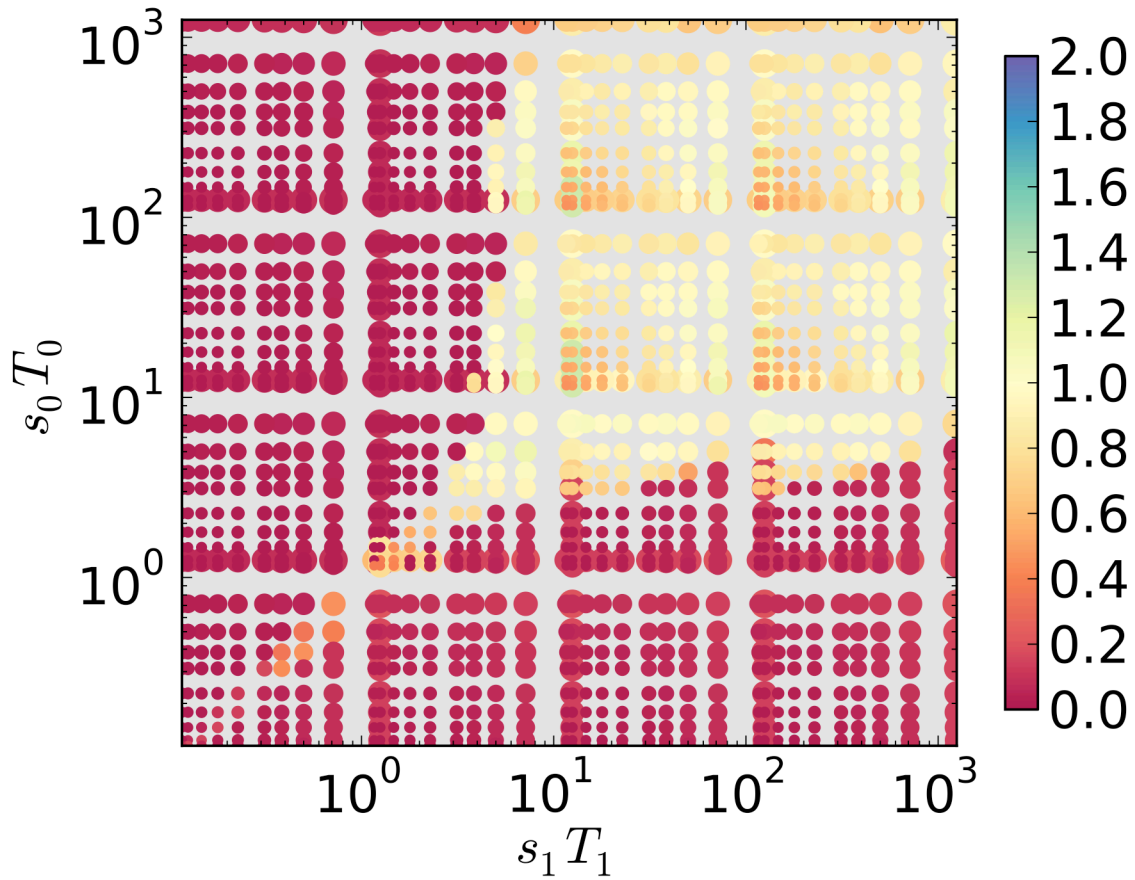
Figure 6 of the main text plots the average winning length for several population sizes: $N=10^7$, $N=10^6$, $N=10^5$, and $N=10^4$. In Supplementary Figure 2, we plot the standard deviations for the same experiments. Drift becomes strong as the population approaches 10^4 , and the standard deviation in the winning length (plotted here) becomes large. For all population sizes, including 10^9 (not shown), there is some variation in the winning lengths in the bottom left corner of the plots (low sT); this is because the indirect selection for mutation rate here is lowest, and drift is relatively strong.



Supplementary Figure 2: When the population size becomes low ($N \sim 10^4$), drift becomes strong, and the standard deviation in the winning length, indicated by the circle colors, becomes large. From top left to bottom right: $N=10^7$, $N=10^6$, $N=10^5$, $N=10^4$.

Halving the parameters a and b

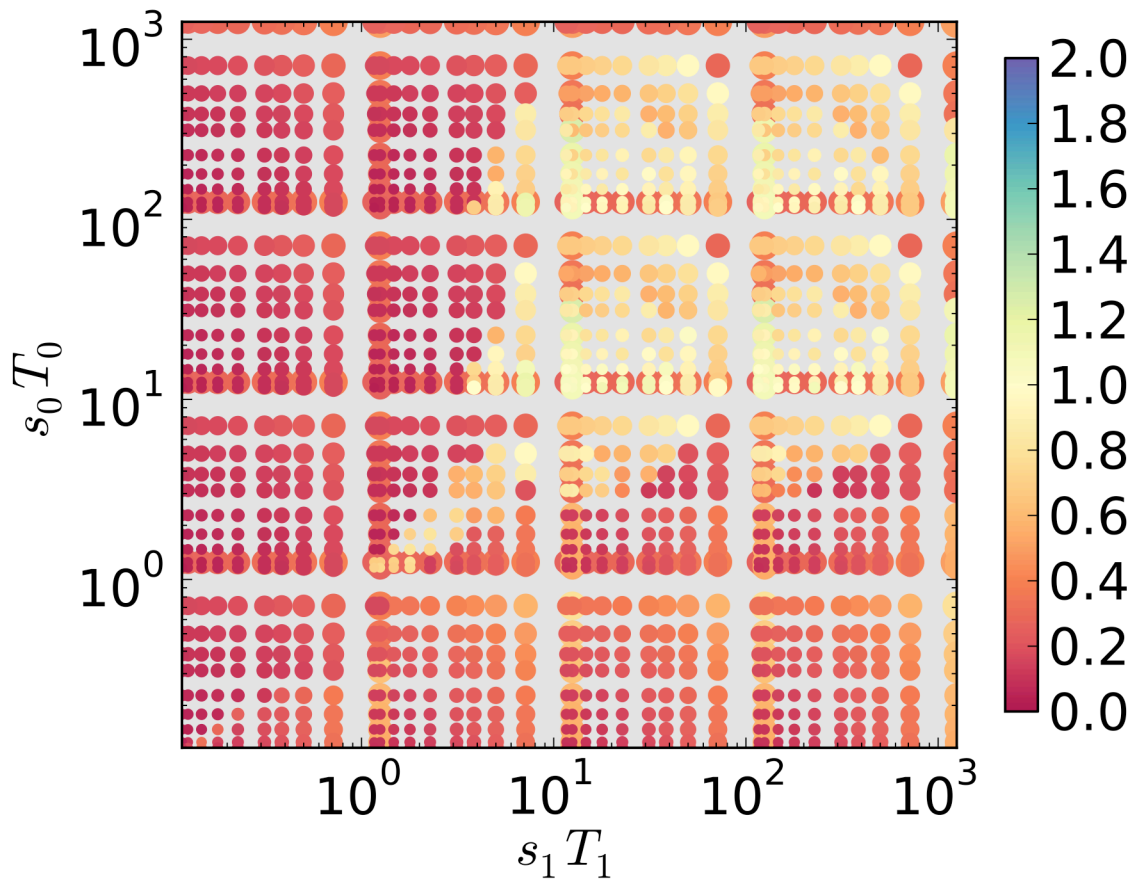
In Supplementary Figure 3, in order to see how the mutation parameters would affect the threshold sT value, we halve the values a and b , to $a=1 \times 10^{-5}$ and $b=1 \times 10^{-4}$ respectively. This effectively halves the mutation rate that corresponds to any length L . The sharp threshold of $s_0 T_0 > 7$ and $s_1 T_1 > 7$, required to favor a non-minimal mutation rate (i.e., points of other than dark red color) still appears.



Supplementary Figure 3: We halved the mutation rate of each length L by halving the parameters a and b . The threshold of $s_0 T_0 > 7$ and $s_1 T_1 > 7$ still applies. The ratio μ_{win}/μ_{avg} is indicated by the color of the circles. $N=10^9$.

Doubling the parameters a and b

In Supplementary Figure 4, we double the values a and b , to $a=4 \times 10^{-5}$ and $b=4 \times 10^{-4}$ respectively. This effectively doubles the mutation rate that corresponds to any length L . In the figure, the darkest red points are slightly more orange than in Figure 5 of the main text; this is because all mutation rates are doubled, so the lowest possible mutation rate is higher. Nonetheless, this minimal mutation rate is still favored at most of the same (s_0, s_1, T_0, T_1) points. The sharp threshold at $s_0 T_0 > 7$ and $s_1 T_1 > 7$, required to favor a non-minimal mutation rate, still appears. Thus, the threshold sT value is insensitive to the parameters a and b .



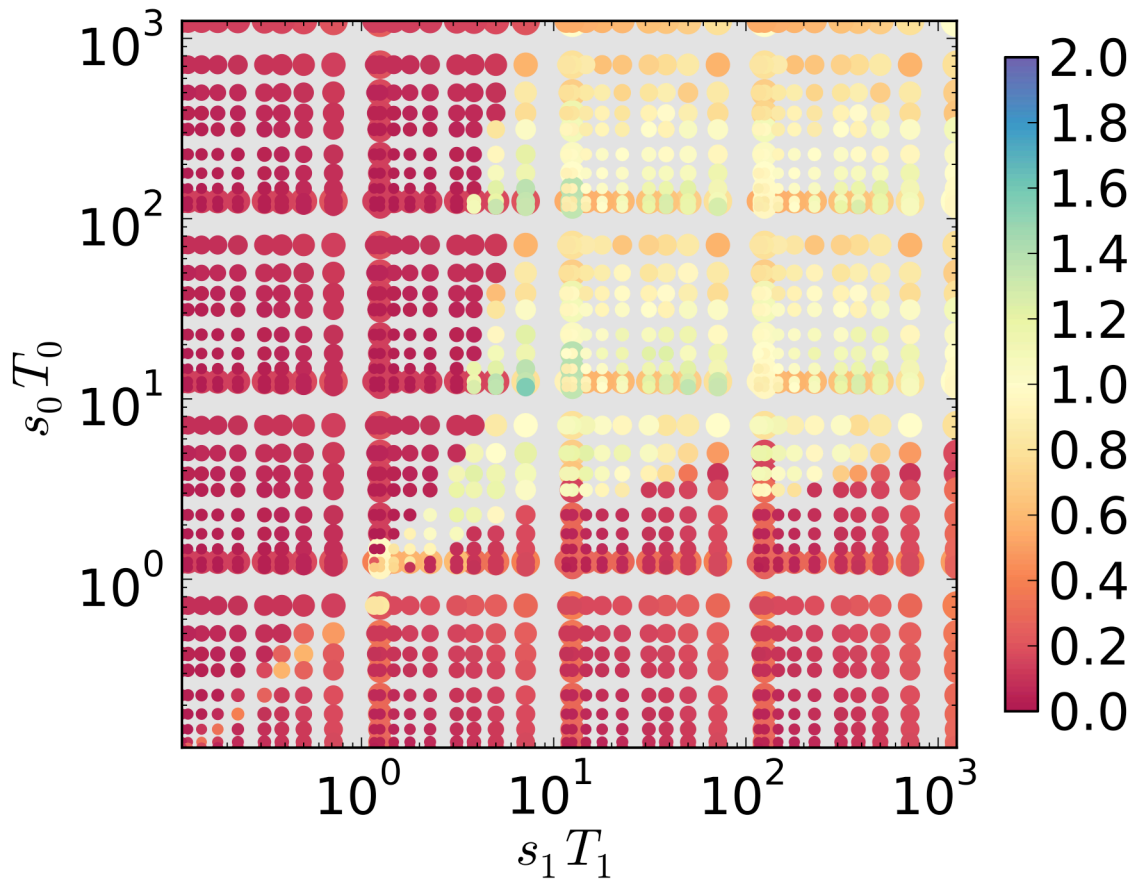
Supplementary Figure 4: We doubled the mutation rate of each length L by doubling the parameters a and b . The threshold of $s_0 T_0 > 7$ and $s_1 T_1 > 7$ still applies. The ratio μ_{win}/μ_{avg} is indicated by the color of the circles. $N=10^9$.

A more constrained mutation kernel

We conducted a set of simulations with an alternate version of the mutation kernel, shown in Supplementary Table 1. The results are plotted in Supplementary Figure 5; changing the mutation kernel in this way does not change the sT threshold.

Length change	Probability
+2	$\mu * 3/63$
+1	$\mu * 18/64$
0	$1 - \mu$
-1	$\mu * 36/63$
-2	$\mu * 6/63$

Supplementary Table 1: A more constrained mutation kernel permitting length changes of only -2 to +2.



Supplementary Figure 5: A different mutation kernel also does not affect the sT threshold. $N=10^9$.