
Figures and figure supplements

Selection on mutators is not frequency-dependent

Yevgeniy Raynes and Daniel Weinreich

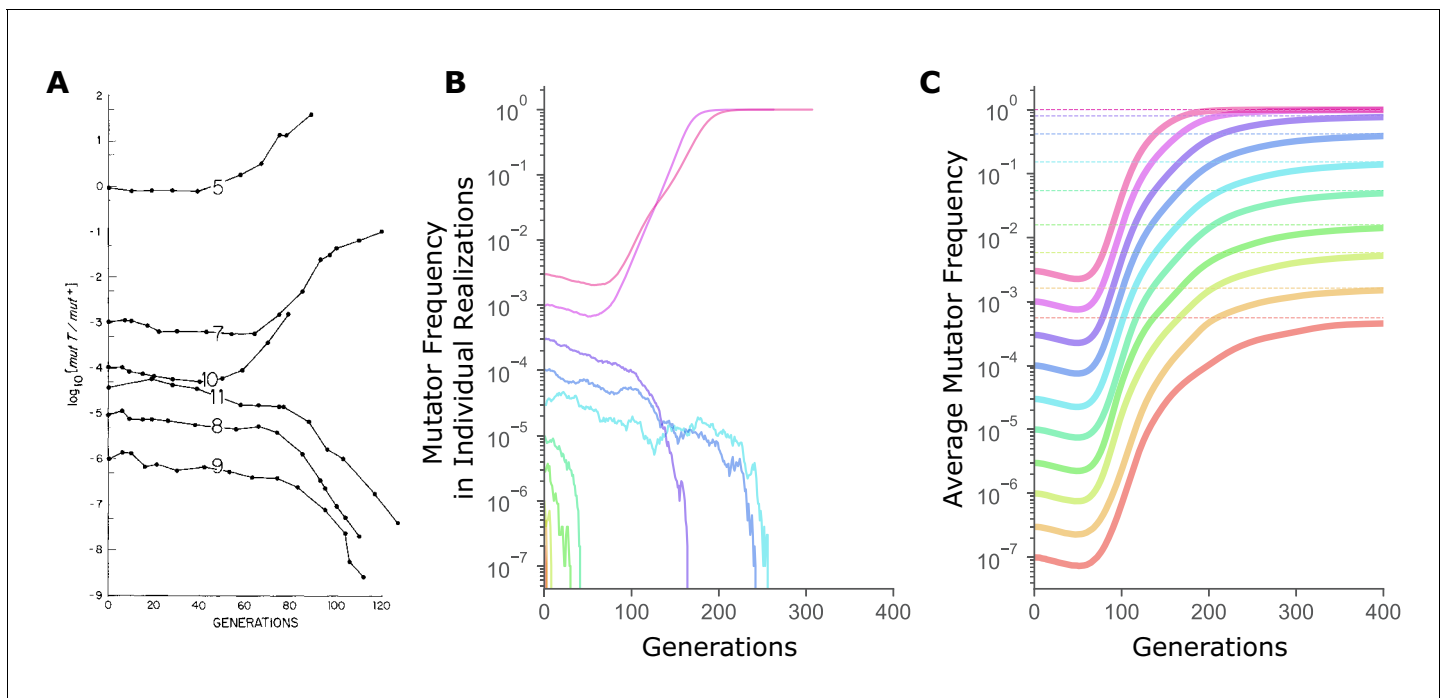


Figure 1. The sharp transition between fixation and loss in mutator dynamics at different starting frequencies is due to limited sampling. (A) Changes in the ratio of the mutator and the wild-type alleles of the *E. coli mutT* locus over time in continuous chemostat cultures. (Figure 1 from **Chao and Cox, 1983**). (B) In simulations, mutator trajectories in individual realizations initiated at different starting frequencies recapitulate the experimental observation of the frequency-threshold for mutator hitchhiking. Parameter values used are typical of microbial experimental populations (**Raynes et al., 2018**): $N = 10^7$, $U_{del} = 10^{-4}$, $U_{ben} = 10^{-6}$, constant $s_{ben} = 0.1$, constant $s_{del} = -0.1$. Mutators mutate 100× faster than non-mutators. (C) Average mutator trajectories across realizations do not show evidence of the frequency-threshold. On average, mutators increase in frequency at all x_0 , showing that selection favors mutators independent of frequency. Average mutator frequency always eventually reaches the expected $P_{fix}(x_0)$ (dashed horizontal lines) calculated in **Figure 2**. Mutator frequencies averaged across 10^6 simulation runs at $x_0 = 10^{-7}$ and $x_0 = 3 \times 10^{-7}$, and across 10^5 simulation runs for all other starting frequencies. For simulations with exponentially distributed selection coefficients see **Figure 1—figure supplement 1**. © 1983 John Wiley and Sons. All Rights Reserved. **Figure 1** reproduced from **Chao and Cox, 1983** with permission.

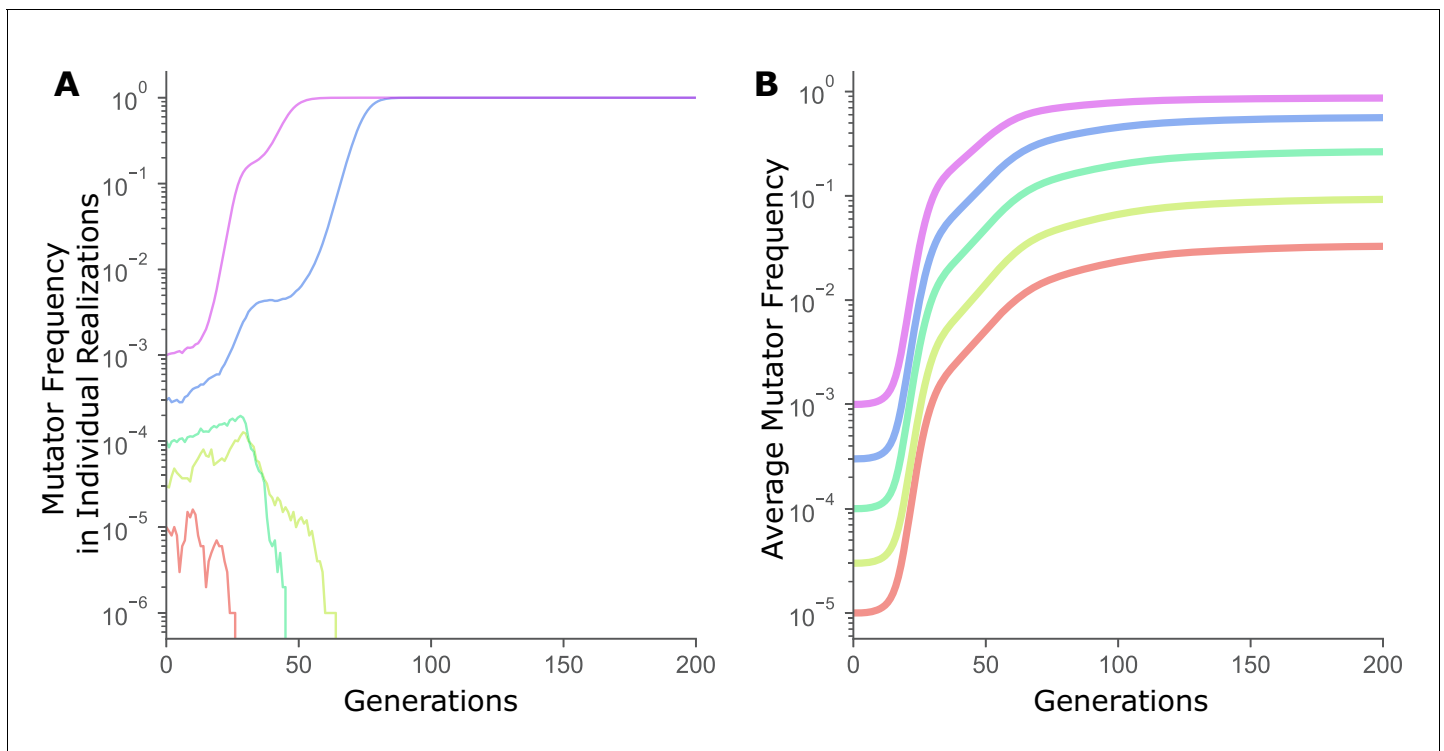


Figure 1—figure supplement 1. Simulations with exponentially distributed selection coefficients confirm that the frequency-dependent threshold in mutator dynamics is due to limited sampling. (A) Mutator trajectories in individual realizations. (B) Average mutator trajectories across realizations. Mutator frequencies averaged across 10^5 simulation runs. Parameter values as in **Figure 1** except $N = 10^6$, and beneficial and deleterious mutations are now randomly drawn from an exponential distribution with the mean $s_{ben} = 0.1$ and $s_{del} = -0.1$ respectively.

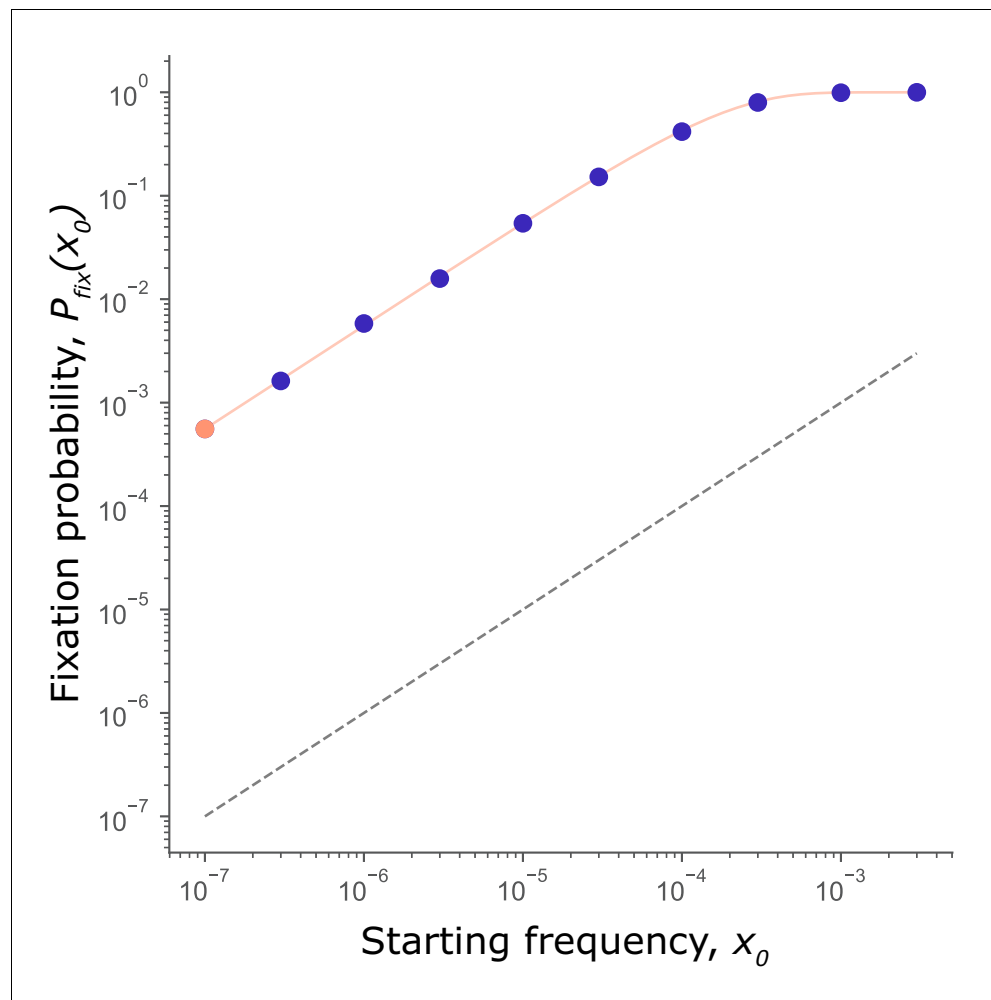


Figure 2. Mutator fixation probability is not frequency-dependent. Fixation probability, $P_{fix}(x_0)$, of a mutator initiated at frequency x_0 (circles: orange for $x_0 = 1/N$, purple for $x_0 > 1/N$). Data from simulations in **Figure 1**. $P_{fix}(x_0)$ scales with but never crosses the fixation probability of a neutral mutation (x_0 ; black dashed line). Thus, mutators are favored at all starting frequencies. The expected fixation probability $P_{fix}(x_0)$ (solid orange line), calculated from the fixation probability of a single mutator, $P_{fix}(x_0 = 1/N) = 5.6 \times 10^{-4}$ (orange point) using **Equation 1** is indistinguishable from the $P_{fix}(x_0)$ observed in simulations, demonstrating that the per-capita fixation probability at every frequency is independent of x_0 and equal to $P_{fix}(x_0 = 1/N)$.

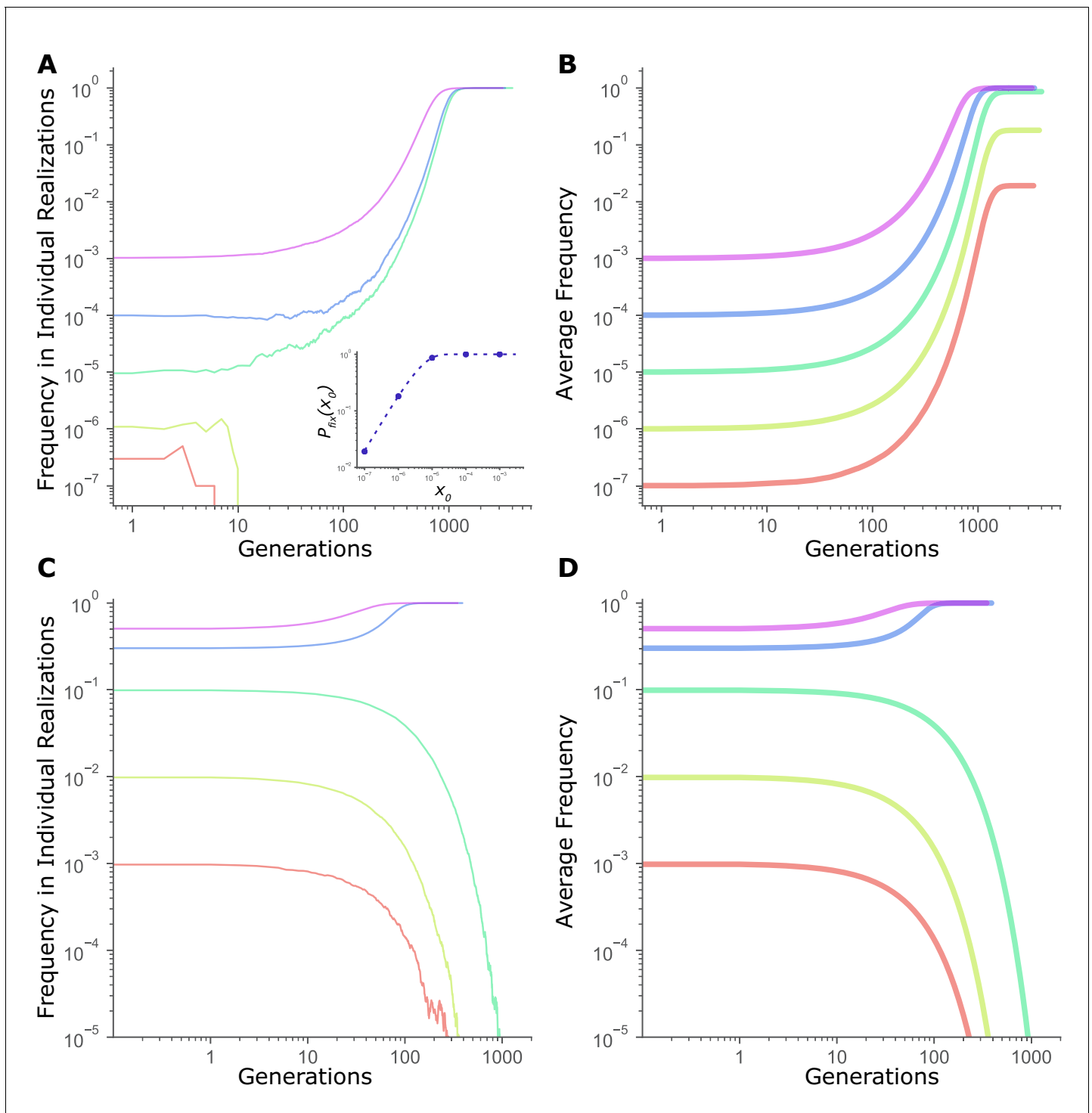


Figure 3. Frequency threshold in dynamics of fitness-affecting mutations. (A) Individual realizations of a simulation initiated with a directly beneficial mutation of size $s_{ben} = 0.01$ at a starting frequency x_0 . Population size, $N = 10^7$. Inset: Fixation probability of a beneficial mutation of size $s_{ben} = 0.01$ at $N = 10^7$. Dashed line is given by $P_{fix}^{ben}(x_0) = \frac{1 - e^{-2s_{ben}N_0}}{1 - e^{-2s_{ben}N}}$ (Kimura, 1962), while circles are values of $P_{fix}^{ben}(x_0)$ measured in simulations (averaged across 10^5 runs). (B) Average frequency trajectories of a beneficial mutation of size $s_{ben} = 0.01$ in (A) averaged across all 10^5 runs of simulation. (C) Individual realizations of a simulation initiated with a mutation under frequency dependent selection, with the selection coefficient $s(x) = b + mx$, where x is the frequency, $b = -0.02$, and $m = 0.1$, at $N = 10^7$. (D) Average frequency trajectories of the frequency-dependent mutation in (C) averaged across all 10^5 runs of simulation. All panels are on a log-log scale for clarity.