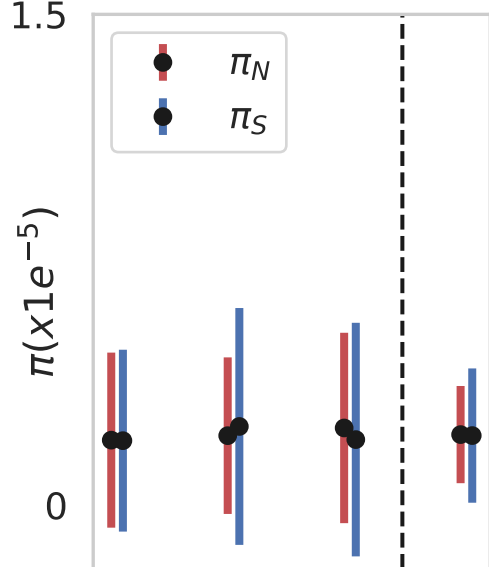
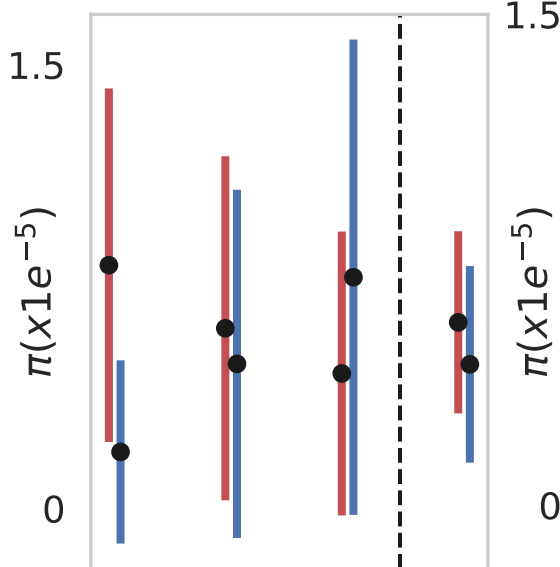


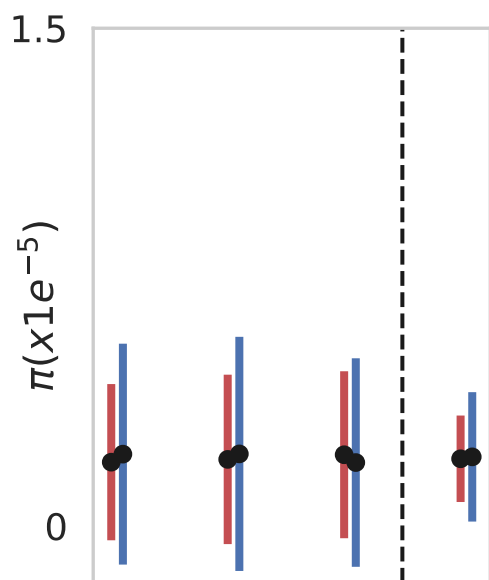
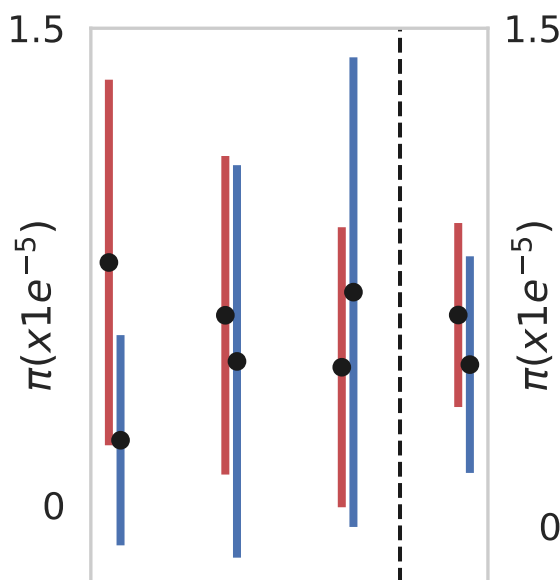
10% of new mutations
are beneficial

1% of new mutations
are beneficial

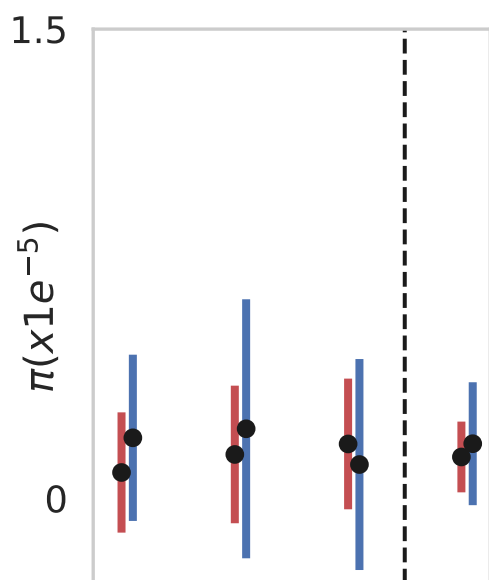
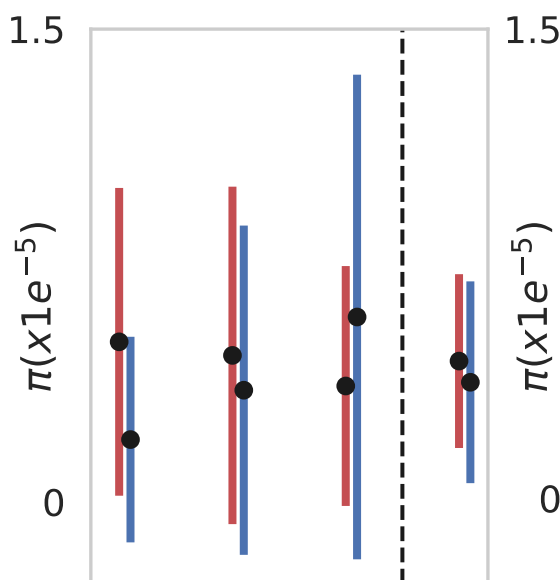
Flynn et al.
experimental
DFE estimates



Weakly
deleterious
background



Strongly
deleterious
background



window 1
window 2
window 3
whole genome

window 1
window 2
window 3
whole genome

Supplementary Figure 1: Per-site π_N and π_S values simulated under recurrent beneficial mutation models, with 10% (left column) and 1% (right column) of mutations experiencing positive selection. These beneficial mutations are occurring on: the CoV-2 DFE experimentally inferred by Flynn *et al.* (2022) (top row), a weakly deleterious DFE as in the above Figures (middle row), and a strongly deleterious DFE as in the above Figures (bottom row). Plots present π_N (red) and π_S (blue) values for 10kb non-overlapping windows, as well as genome-wide (30kb) values. All other parameter details are as in Figure 1, except mutation rate/site/replication= $2.135e-7$ and carrying capacity= $1e3$, in order to achieve ~ 5 SNPs per sampled genome at $>2.5\%$ frequency (as in the empirical data) under these recurrent positive selection models (*i.e.*, the large input of beneficial mutations necessitates a reduced mutation rate relative to the above figures, in order to maintain levels of variation consistent with the published patient data). Source data are provided as a Source Data file. All code for replicating these results is available on GitHub (https://github.com/vivaksoni/Gu_etal_2023_response).