

Figure S1 Comparison of different grids. Shown are the cumulative probability density distributions (CDF) of allele frequencies after 10, 100 and 1000 generations (shown in top left corner) of selection and random drift starting from a frequency of 0.2 and obtained under the Wright-Fisher diffusion (black) and the *mean transition time* approximation for 51 and 21 uniform (solid) or quadratic (dashed) states. Results are shown for small ($N = 100$, A and B) and large ($N = 10,000$, C and D) population sizes and weak ($s = 0.01$, A and C) and strong ($s = 0.3$, B and D) selection.

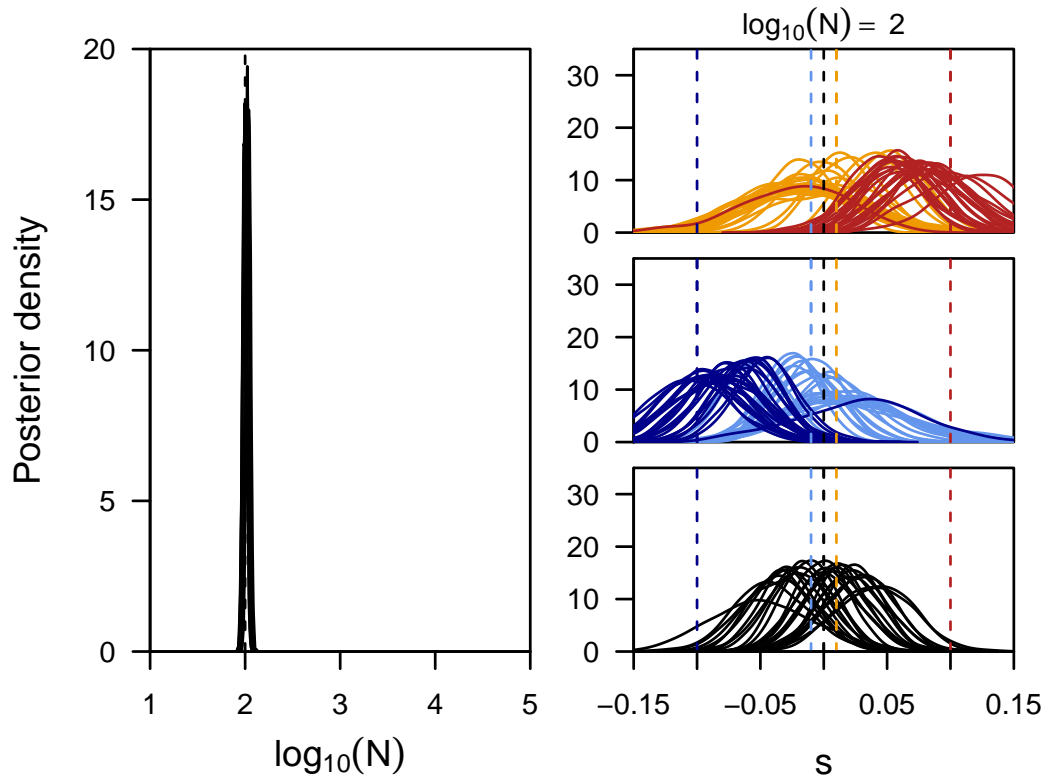


Figure S2 Power to infer selection and population size jointly. Here we show the posterior distributions on the population size (first panel) and locus-specific selection coefficients obtained for five replicate simulations for each of three different population sizes. For each replicate we plot the posteriors of all loci simulated under selection (color) as well as five neutral loci picked at random (black). In contrast to the results shown in the main text, the data was simulated here with more ideal starting frequencies, namely 0.1, 0.5 and 0.9 for positively selected, neutral and negatively selected sites, respectively.

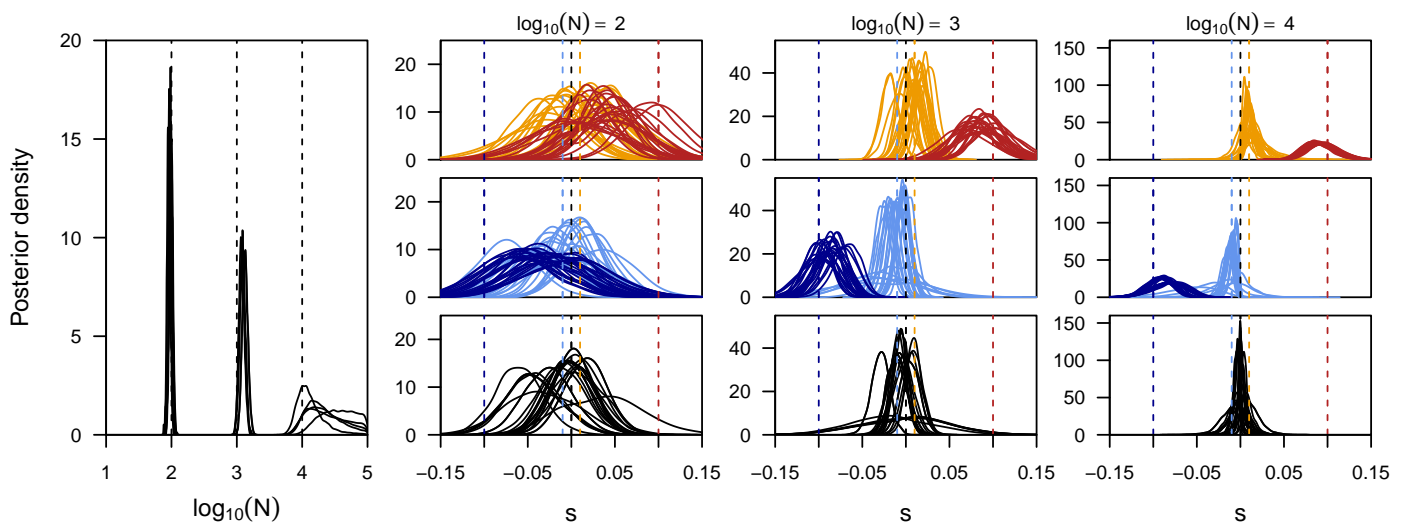


Figure S3 Power to infer selection and population sizes jointly. Here we show the posterior distributions on the population size (first panel) and locus-specific selection coefficients obtained for five replicate simulations for each of three different population sizes. For each replicate we plot the posteriors of all loci simulated under selection (color) as well as five neutral loci picked at random (black). In all simulations, starting frequencies were chosen randomly for each locus. In contrast to the results shown in the main text, 80% of all simulated loci were affected by selection.

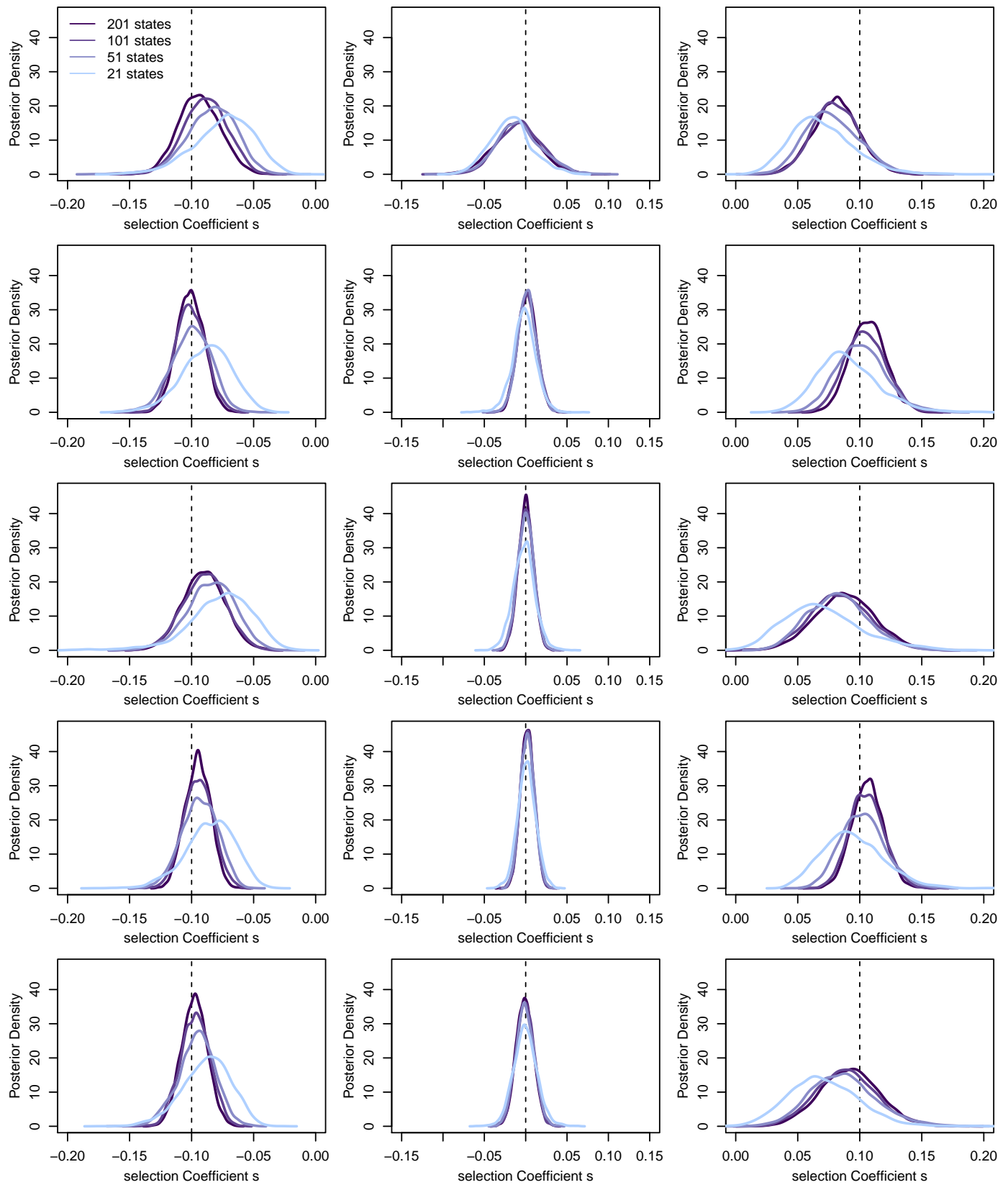


Figure S4 Power to infer selection as a function of the number of states. We simulated five independent loci for each of the three selection coefficients $s = -0.1$, $s = 0$ and $s = 0.1$ for a population size of $\log_{10}(N) = 4$. We then inferred the posterior distributions on s for each locus using different numbers of states, but assuming $\log_{10}(N) = 4$. Estimates are generally biased towards weaker selection when using too few states.

Table S1 Sites found to be under selection in Influenza

| Segment | Position | Ancestral ^a | Derived | Protein Change ^b | s ^c |
|---------|----------|------------------------|---------|-----------------------------|----------------------|
| PB2 | 185 | AGG | AAG | R61K | -0.08 (-0.18, -0.02) |
| PB2 | 282 | TCG | TCA | S94 | -0.05 (-0.10, -0.02) |
| PB2 | 912 | GAA | GAG | E304 | -0.08 (-0.18, -0.01) |
| PB2 | 1225 | CGT | AGT | R408S | 0.08 (0.01, 0.16) |
| PB2 | 1629 | GAG | GAA | E543 | -0.09 (-0.18, -0.03) |
| PB2 | 1890 | AGA | AGG | R630 | -0.07 (-0.19, -0.02) |
| PB2 | 2299 | - | - | - | 0.06 (0.01, 0.12) |
| PB2 | 2300 | - | - | - | 0.05 (0.02, 0.11) |
| PB2 | 2304 | - | - | - | 0.07 (0.02, 0.13) |
| PB1 | 33 | AAA | AAG | K11 | 0.12 (0.07, 0.18) |
| PB1 | 529 | GGT | AGT | G176S | -0.12 (-0.22, -0.04) |
| PB1 | 1365 | AAT | AAC | N455 | 0.07 (0.01, 0.15) |
| PB1 | 2034 | AGT | AGC | S678 | -0.06 (-0.12, -0.03) |
| PA | 90 | ACT | ACA | T30 | -0.08 (-0.17, -0.01) |
| PA | 174 | GGT | GGG | G58 | -0.14 (-0.23, -0.07) |
| PA | 178 | CTA | GTA | L59V | -0.03 (-0.05, -0.01) |
| PA | 1614 | GAG | GAA | E538 | 0.09 (0.03, 0.16) |
| PA | 2193 | - | - | - | 0.06 (0.02, 0.13) |
| PA | 2194 | - | - | - | 0.07 (0.04, 0.12) |
| PA | 2196 | - | - | - | 0.07 (0.03, 0.13) |
| HA | 48 | CCG | TCG | P6S* | 0.17 (0.12, 0.25) |
| HA | 639 | AAT | GAT | N203D | -0.11 (-0.19, -0.06) |
| HA | 640 | AAT | ACT | N203T | -0.13 (-0.21, -0.07) |
| HA | 1023 | GCC | ACC | A331T | -0.09 (-0.19, -0.02) |
| HA | 1196 | ACC | ACT | T388 | -0.10 (-0.18, -0.02) |
| HA | 1395 | AAT | GAT | N455D | 0.21 (0.15, 0.29) |
| HA | 1601 | CTA | CTG | L523 | -0.09 (-0.18, -0.02) |
| HA | 1760 | - | - | - | 0.02 (0.01, 0.06) |
| NP | 25 | CTC | ATC | L8I | -0.05 (-0.11, -0.02) |
| NP | 390 | ATG | ATA | M130I | -0.12 (-0.21, -0.06) |
| NP | 1104 | AAC | AAT | N368 | -0.11 (-0.21, -0.05) |
| NA | 143 | ACA | ATA | T47I | 0.09 (0.04, 0.16) |
| NA | 582 | GGA | GGG | G194* | 0.23 (0.16, 0.30) |
| NA | 823 | TAC | CAC | Y274H | 0.20 (0.14, 0.27) |
| NA | 978 | TTG | TTC | L326F | -0.05 (-0.12, -0.01) |
| NA | 1427 | - | - | - | -0.13 (-0.22, -0.05) |
| M1/2 | 92 | GAG | TAG | E22stop* | -0.06 (-0.14, -0.01) |
| M1/2 | 147 | GTC | GCC | V41A | 0.13 (0.08, 0.18) |
| M1/2 | 848 | TGT | TGG | C274W | -0.07 (-0.16, -0.02) |
| NS1/2 | 201 | AGG | AGA | R67 | 0.08 (0.03, 0.15) |
| NS1/2 | 329 | AAA | AGA | K109R | 0.07 (0.01, 0.14) |
| NS1/2 | 373 | GAC | AAC | D124N | -0.09 (-0.18, -0.02) |
| NS1/2 | 820 | - | - | - | 0.13 (0.08, 0.20) |

^a Ancestral codon refers to the allele with the highest frequency at the beginning of the experiment (passage 0). Dashes indicate mutations in non-coding regions

^b Protein changes are reported in standard nomenclature but comparing the derived codon to the ancestral codon (not the published reference).

^c Reported is the posterior median of the locus-specific selection coefficient, along with the 99% credible interval.