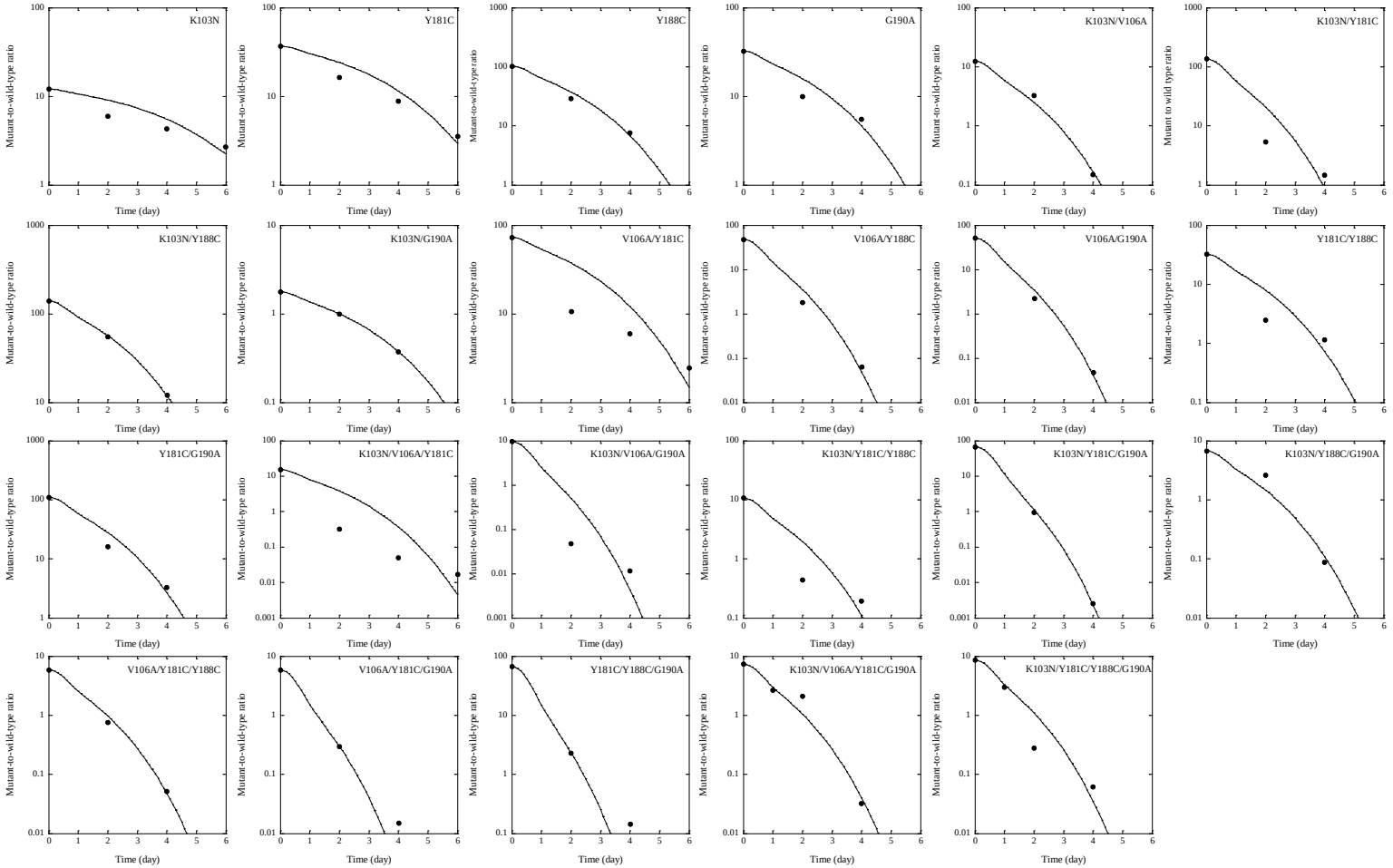

Figure S1. Fits of our model (Eq. 1) (lines) to data (symbols) from competitive growth assays (8) for different mutants. Collins et al. (8) found that a triple mutant, two quadruple mutants, and the quintuple mutant were unviable. We set the relative fitness of the latter mutants to zero.

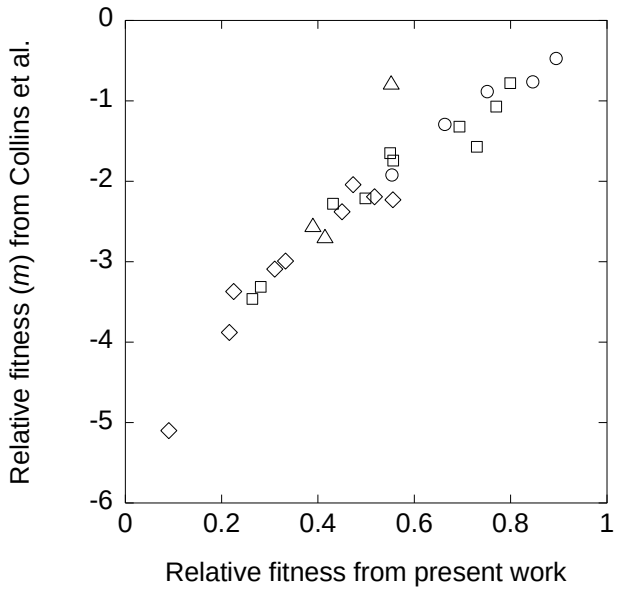

Figure S2. Comparisons of the relative fitness of viable single (circles), double (squares), triple (diamonds), and quadruple (triangles) mutants estimated by Collins et al. (8) and by our present fits (Fig. 2).

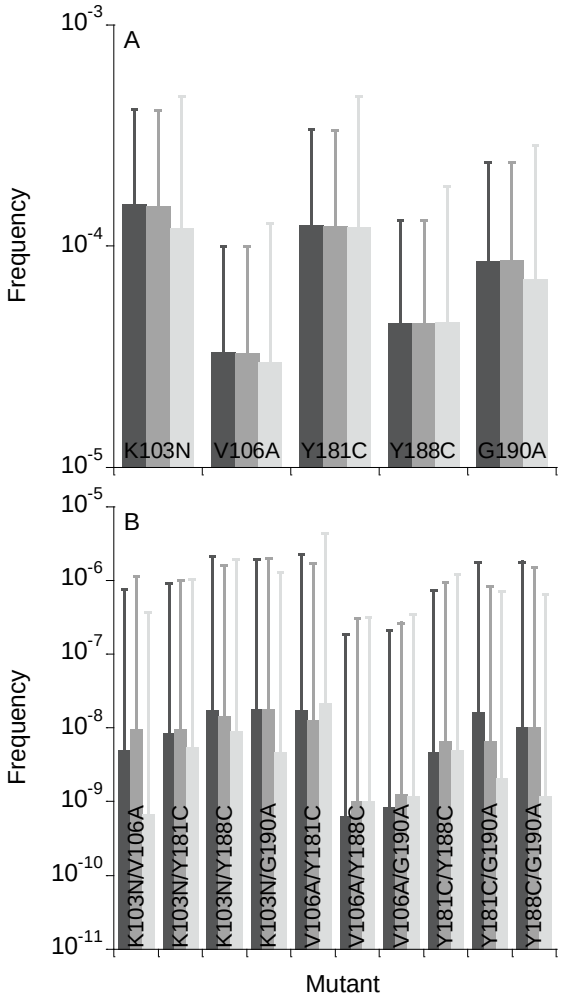

Figure S3. The expected frequencies of single (A) and double (B) mutants in cell-free viral RNA corresponding to the frequencies in proviral DNA shown in Fig. 6.

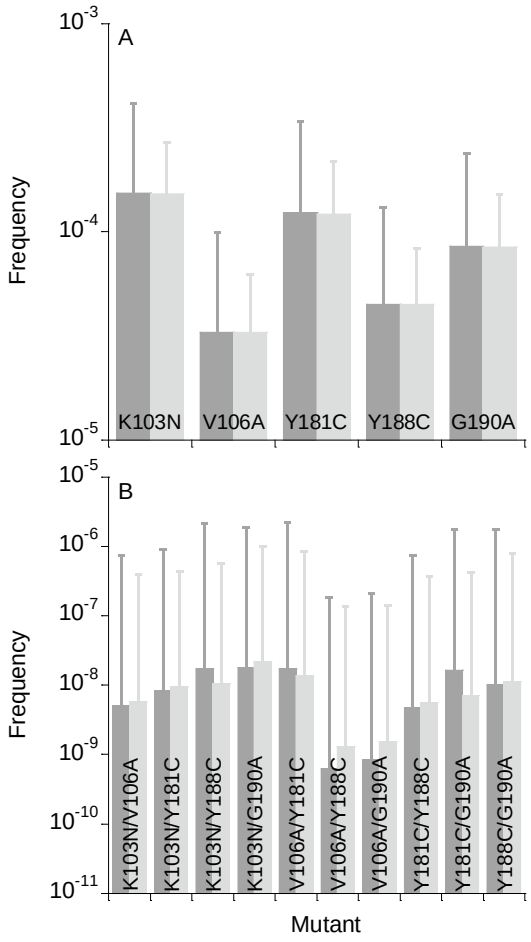

Figure S4. The expected frequencies of single (A) and double (B) mutants in cell-free viral RNA corresponding to the frequencies in proviral DNA shown in Fig. 7.

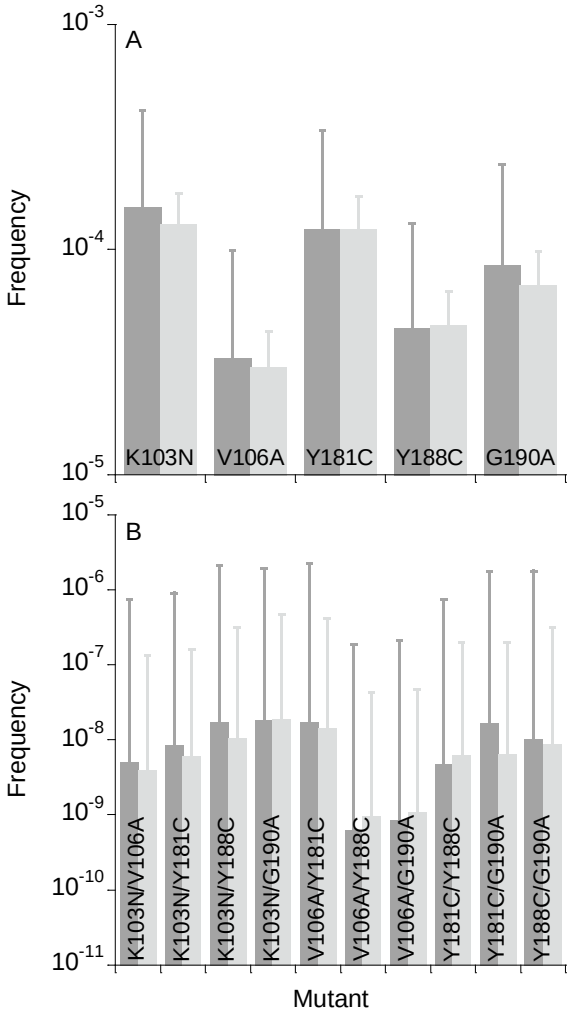

Figure S5. The expected frequencies of single (A) and double (B) mutants in cell-free viral RNA corresponding to the frequencies in proviral DNA shown in Fig. 8.

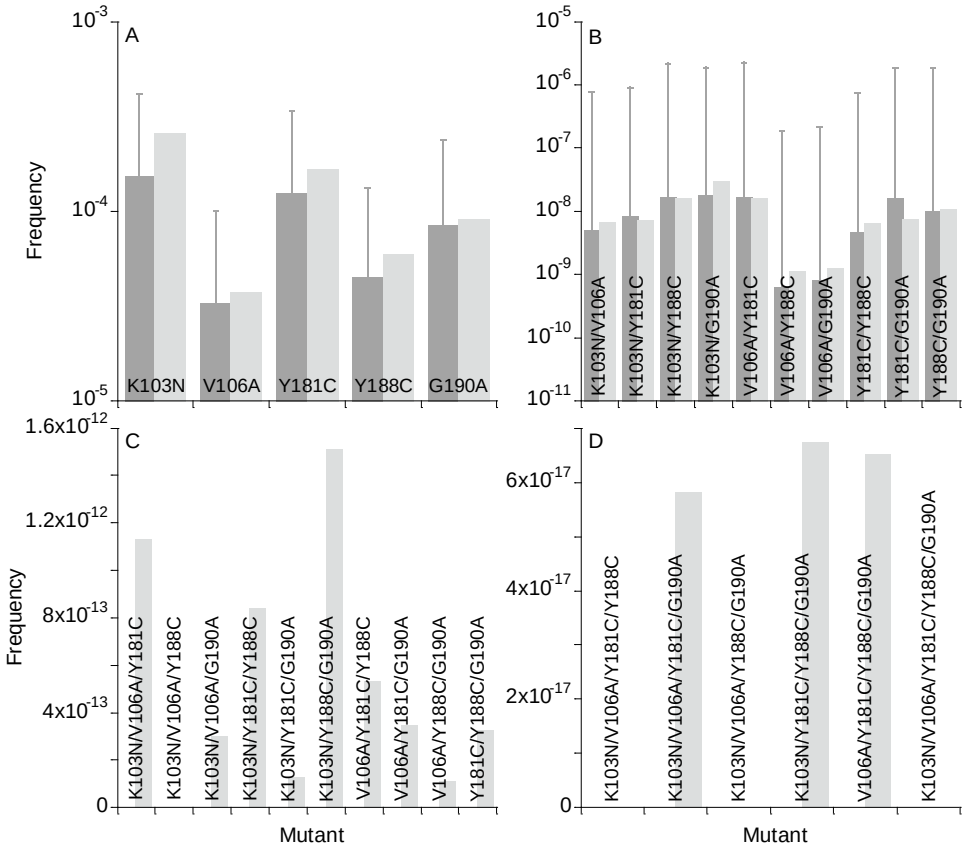

Figure S6. The expected frequencies of single (A), double (B), triple (C) and quadruple and quintuple (D) mutants in cell-free viral RNA corresponding to the frequencies in proviral DNA shown in Fig. 9.

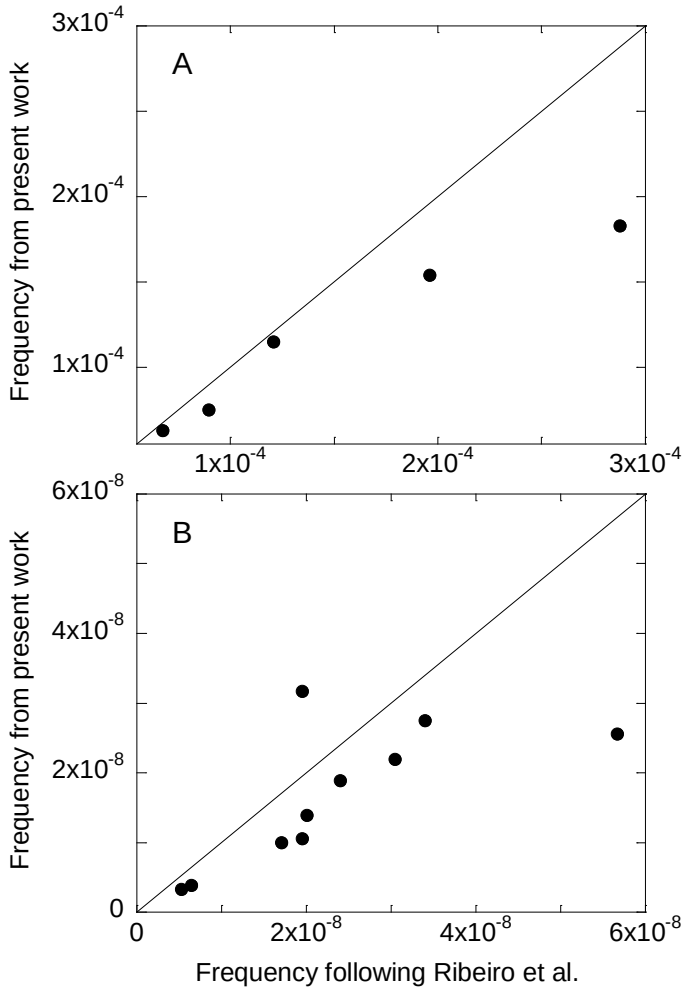

Figure S7. The expected frequencies of single (A) and double (B) mutants estimated from our simulations (Fig. 5) (symbols) shown versus the corresponding frequencies computed following Ribeiro et al. (48). The latter computation is performed as follows. In the nomenclature of Ribeiro et al. (48), when mutations at two loci are considered, 00 represents the wild-type, 01 and 10 single mutants, and 11 the double mutant. The frequencies of the different strains in the proviral DNA are then $\phi_{01}^C / \phi_{00}^C = \mu / (1-\zeta_{01})$, $\phi_{10}^C / \phi_{00}^C = \mu / (1-\zeta_{10})$, and $\phi_{11}^C / \phi_{00}^C = \mu^2 (1-\zeta_{11})^{-1} \left((1-\zeta_{01})^{-1} + (1-\zeta_{10})^{-1} - 1 \right)$, where the ζ's represent the corresponding relative fitness values. That the data lie predominantly below the $y=x$ lines (solid lines) indicates that our simulations predict frequencies smaller than those estimated

following Ribeiro et al. (48). Indeed, we find that the double mutant frequencies from our simulations are significantly smaller than those estimated following Ribeiro et al. (48) (P=0.04 from a one-tailed, paired T-test). (For the single mutants, we find the corresponding P=0.07.) At the same time, we find that the double mutant frequencies estimated by our simulations are not significantly different from those estimated by our deterministic model (Fig. 9) (P=0.41).