Validation of natural populations 6 5 Bootstrapped model - naive distance to future (AAs) -0.72 +/- 0.30 AAs -0.58 +/- 0.17 AAs -0.56 +/- 0.17 AAs -0.39 +/- 0.17 AAs -0.27 +/- 0.14 AAs -0.26 +/- 0.11 AAs 0.20 +/- 0.21 AAs 0.34 +/- 0.34 AAs 0.49 +/- 0.26 AAs 0.73 +/- 0.24 AAs -0.95 +/- 0.29 AAs p = 0.0005p = 0.0059p = 0.0003p = 0.0004p = 0.0136p = 0.0264p = 0.0146p = 0.8344p = 0.8501p = 0.9683p = 0.9989-2 mutational load + LBI mutational load + delta frequency mutational load DMS mutational mutational load + HI antigenic novelty mutational load + mutational load + epitope antigenic LBI effects HI antigenic novelty HI antigenic novelty + epitope ancestor epitope antigenic novelty LBI novelty Model Test of natural populations 0.08 +/- 0.33 AAs 0.89 +/- 0.64 AAs 1.60 +/- 0.79 AAs -0.85 +/- 0.41 AAs -0.83 +/- 0.41 AAs -0.61 +/- 0.33 AAs -0.29 +/- 0.23 AAs -0.29 +/- 0.23 AAs 0.99 +/- 0.49 AAs -0.36 +/- 0.30 AAs -0.12 +/- 0.27 AAs p = 0.5889p = 0.1034p = 0.9263p = 0.9938p = 0.0080p = 0.0108p = 0.0085p = 0.1100p = 0.9836p = 0.1186p = 0.32235 Bootstrapped model - naive distance to future (AAs) mutational load + LBI mutational load + mutational load + HI antigenic novelty mutational load mutational load + DMS mutational mutational load + delta frequency epitope antigenic LBI effects HI antigenic novelty HI antigenic novelty + epitope ancestor epitope antigenic novelty LBI novelty

Model