Validation of simulated populations Bootstrapped model - naive distance to future (AAs) p < 0.0001p = 0.8826true fitness mutational load + LBI mutational load + mutational load delta frequency mutational load + epitope antigenic LBI epitope ancestor epitope antigenic novelty novelty Model Test of simulated populations Bootstrapped model - naive distance to future (AAs) p < 0.0001p < 0.0001p < 0.0001p = 0.0404p < 0.0001p < 0.0001p < 0.0001p = 0.4506true fitness mutational load + LBI delta frequency mutational load + mutational load mutational load + epitope antigenic LBI epitope ancestor epitope antigenic novelty novelty Model