**Figure S16.**—Evolution of constraint (left) and occupancy (right) over time for enhancer 4 (replicates 1-3). See Figures 2 and 5 for complete legend details and labels for the constraint and occupancy plots respectively. In brief, the rows corresponds to the successive enhancers formed by each substitution along the lineage leading to the most common haplotype at the end of the simulation, one row per haplotype. Time proceeds down the vertical axis. The horizontal axis corresponds to the enhancer nucleotides. For each haplotype, the positions (along the horizontal axis) are colored according to $N\bar{s}$ in the left-hand plots and according to max occupancy in the right-hand plots. Red circles indicate the locations of substitutions. This simulation is without indels.