

Supplementary figure 1

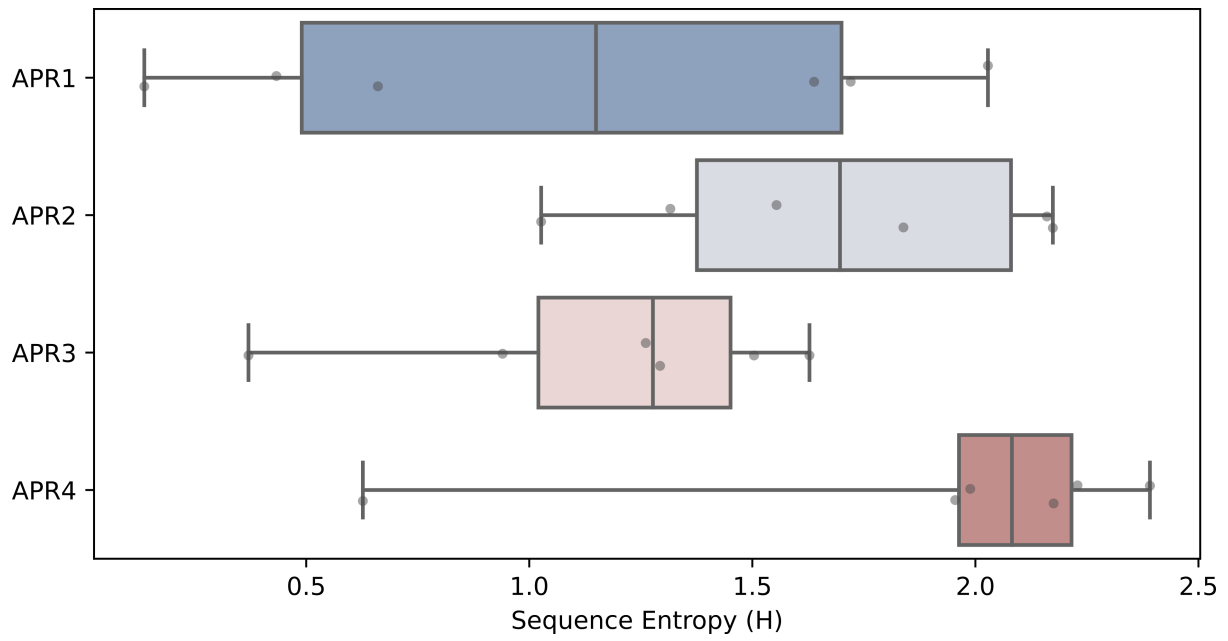


Figure 1: APRs Shannon's entropy (H) content.

Supplementary figure 2

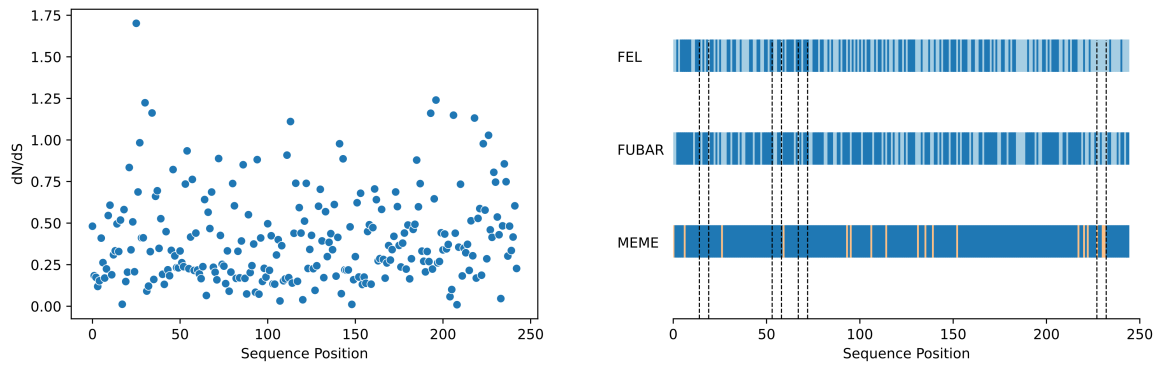


Figure 2: Evolutionary rate (dN/dS) for each residue in the apoA-I codon alignment (left panel). Cartoon depicting the evidence of adaptive evolution for each site of apoA-I sequence (right panel). Residues under purifying, neutral and diversifying selection are colored in blue, paleblue and orange, respectively.

Supplementary figure 3

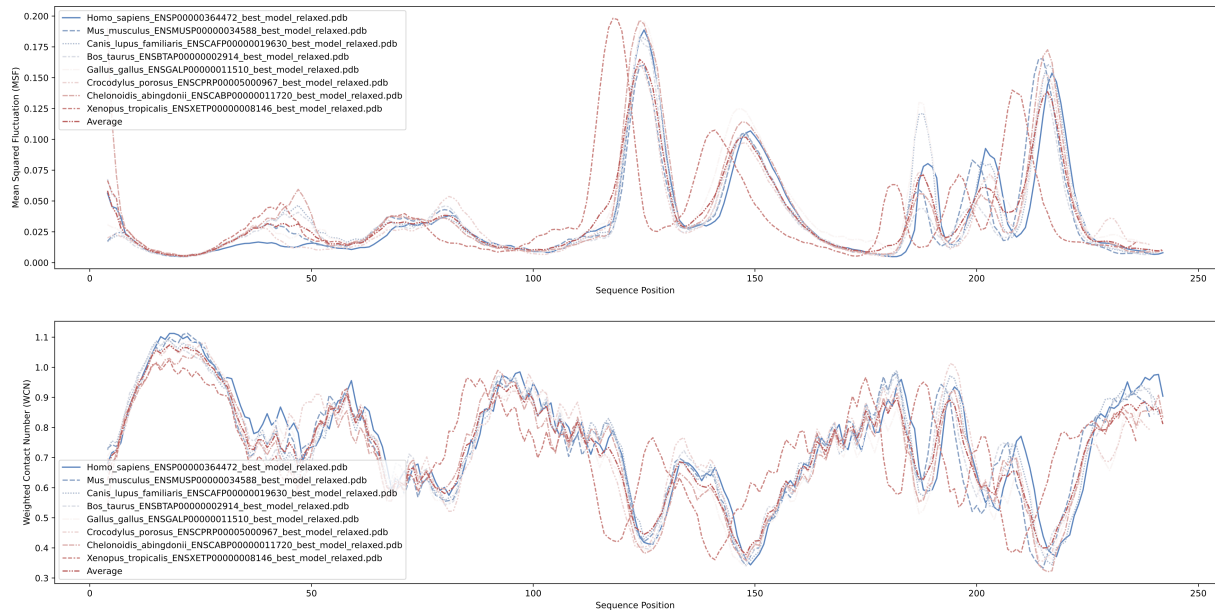


Figure 3: Mean squared fluctuation (MSF, upper panel) and weighted contact number (WCN, lower panel) profiles computed for each modelled structure

Supplementary figure 4

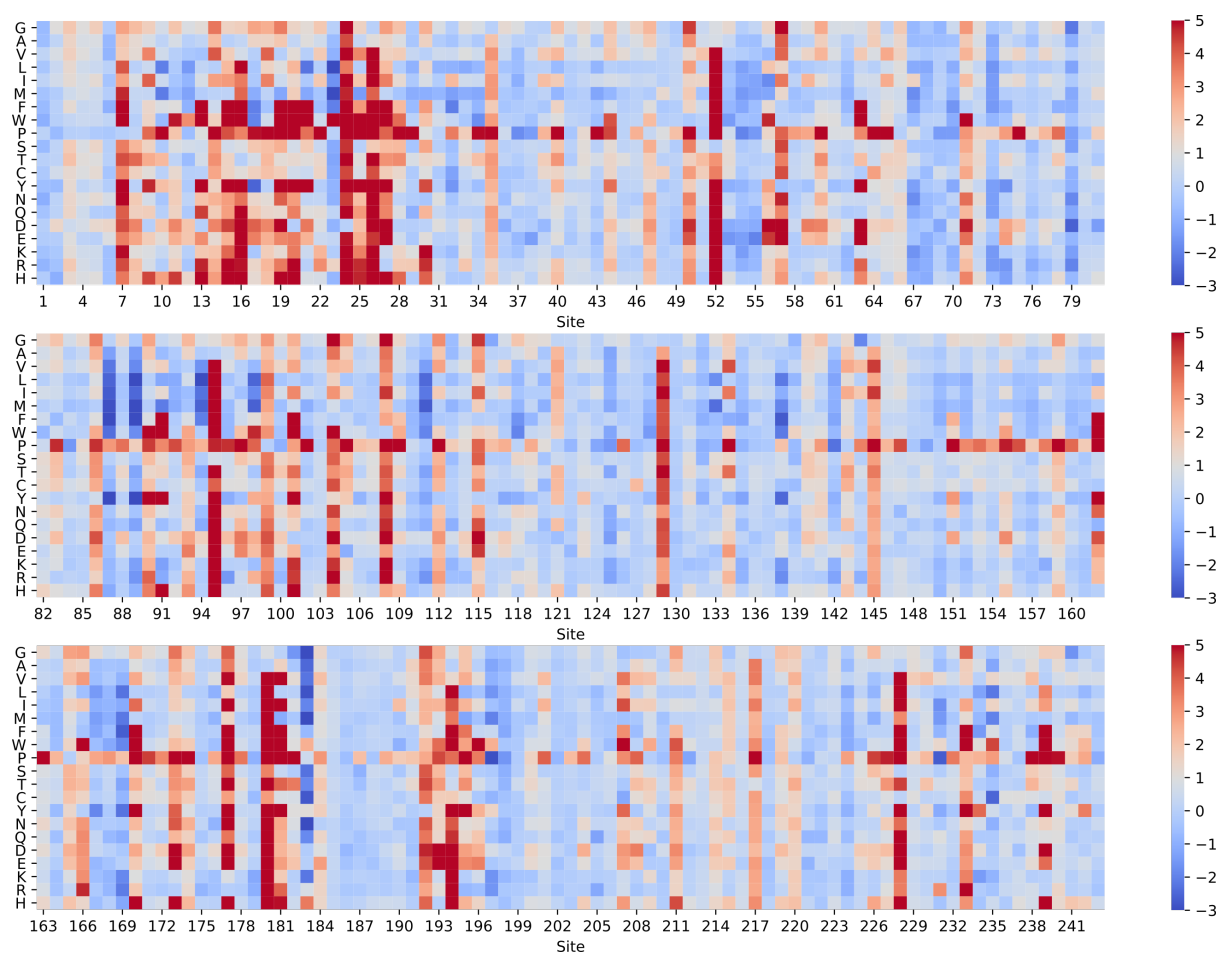


Figure 4: FoldX thermodynamic destabilization landscape. $\Delta\Delta G$ values obtained by *in silico* saturation mutagenesis of apoA-I structure using the FoldX engine. Mutation introduced is depicted in the Y axis. Scales at the right indicate $\Delta\Delta G$ values expressed in kcal/mol.

Supplementary figure 5

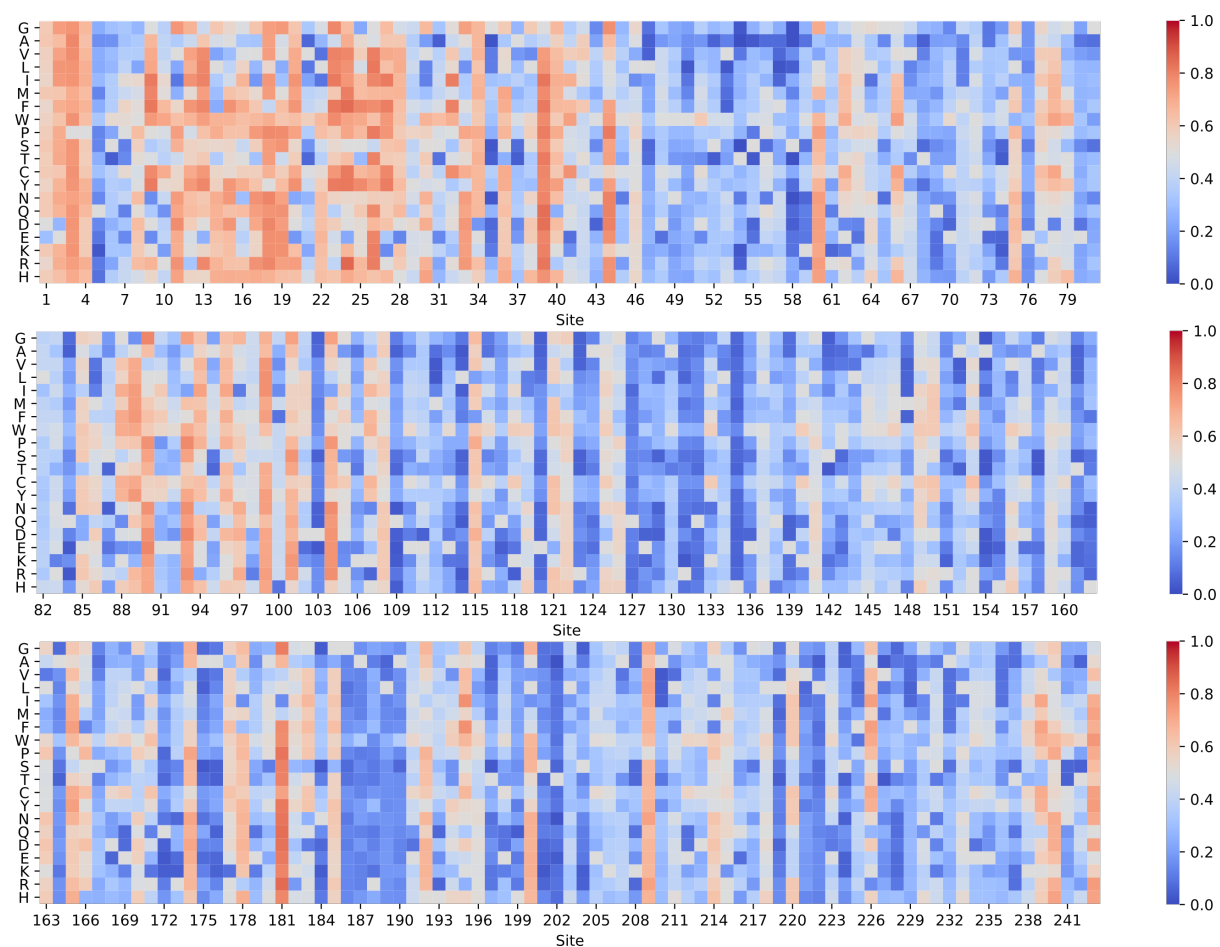


Figure 5: Rhapsody pathogenicity landscape. Pathogenicity values obtained by *in silico* saturation mutagenesis of apoA-I structure using the Rhapsody package. Mutation introduced is depicted in the Y axis. Scales at the right indicate pathogenicity score (1 more pathogenic, 0 less pathogenic)

Supplementary figure 6

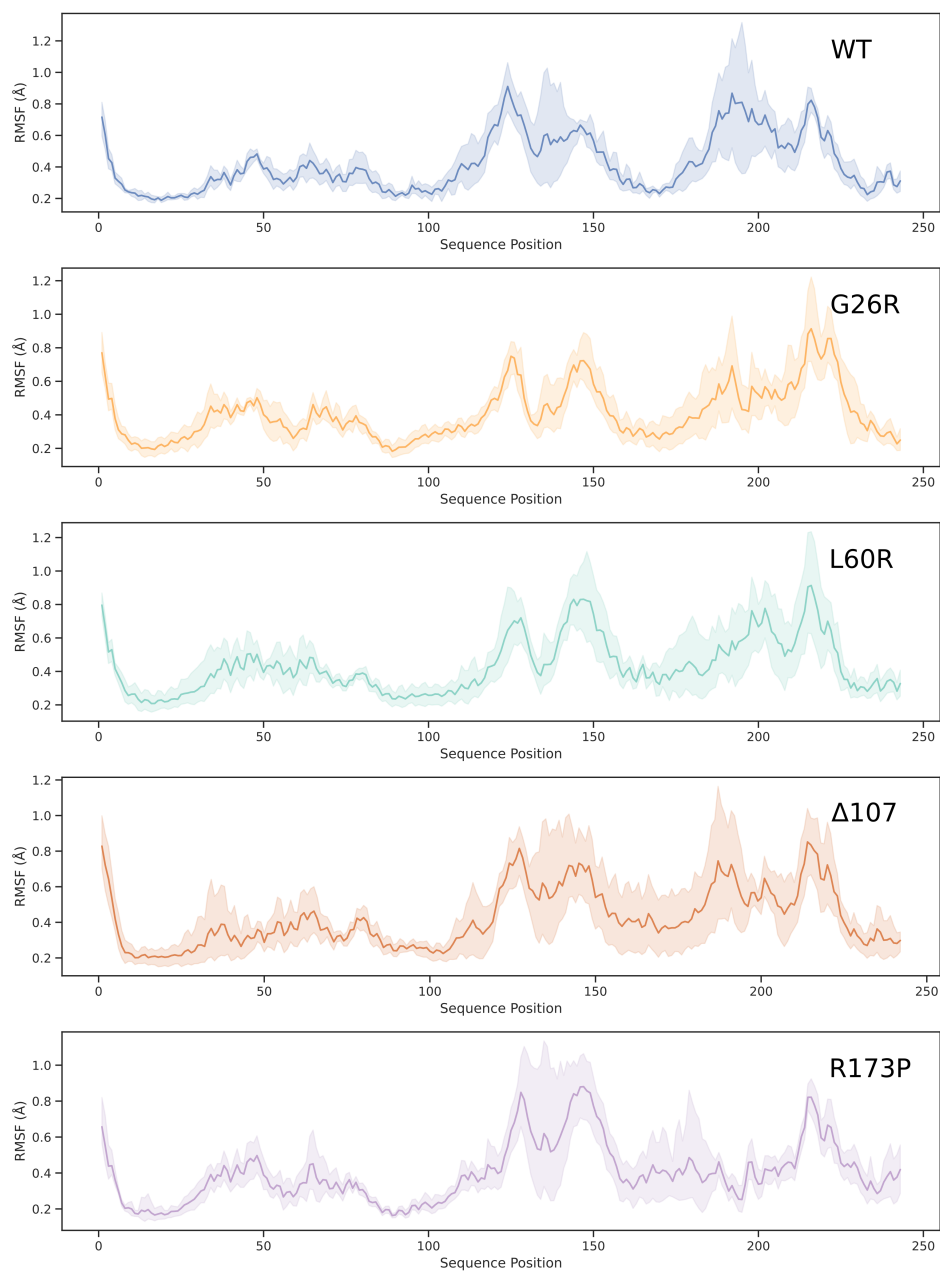


Figure 6: Root mean square fluctuation (RMSF) profiles for apoA-I mutants. RMSF values were computed for each protein position over the last 100 ns of the simulation. Mean values are depicted together with its standard deviation.