Purifying Selection Against AP1 Site Completion
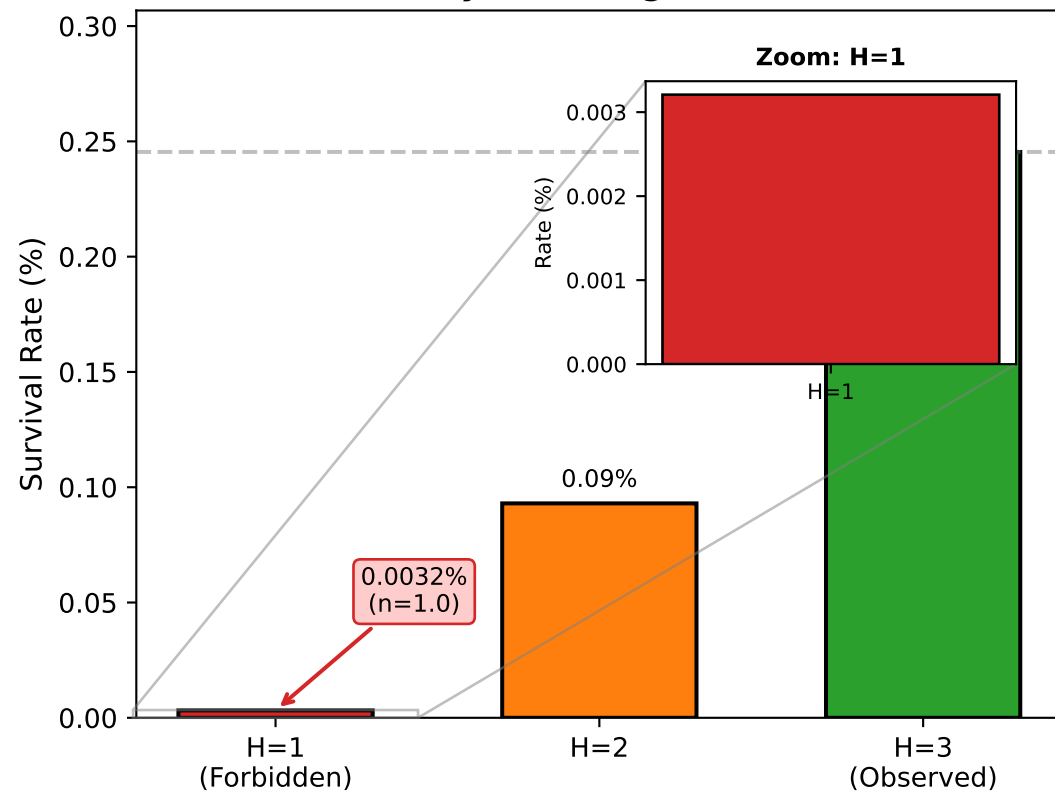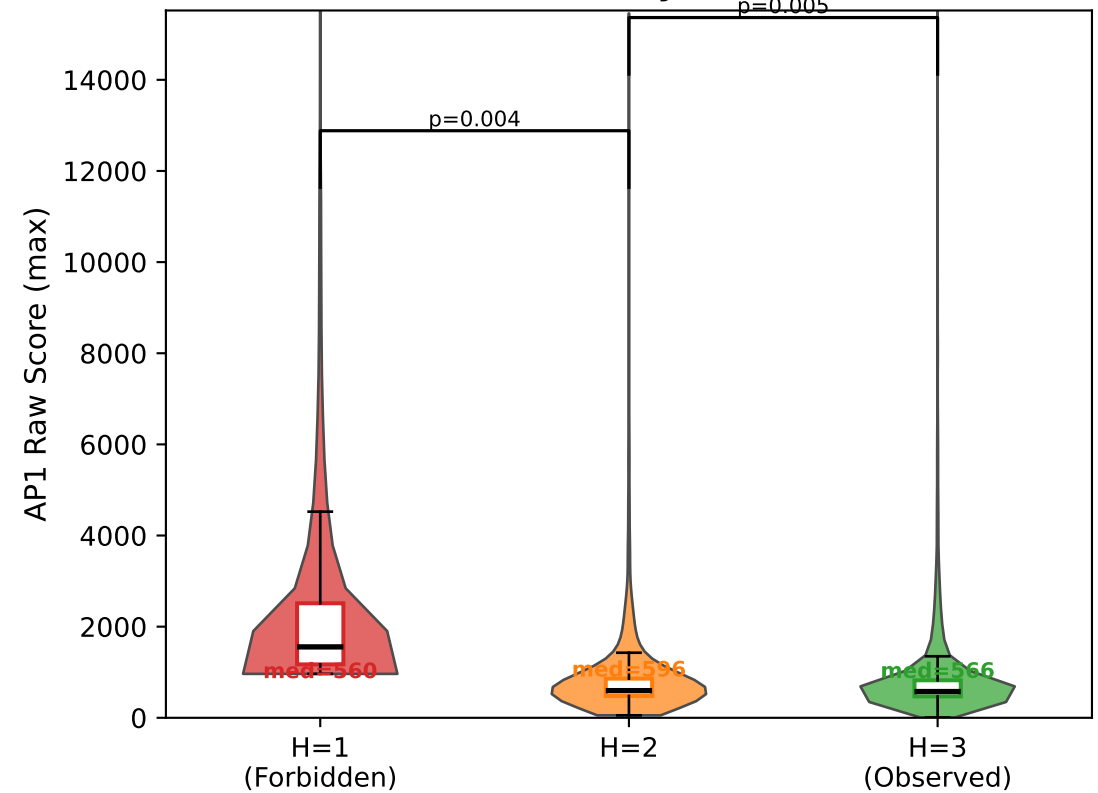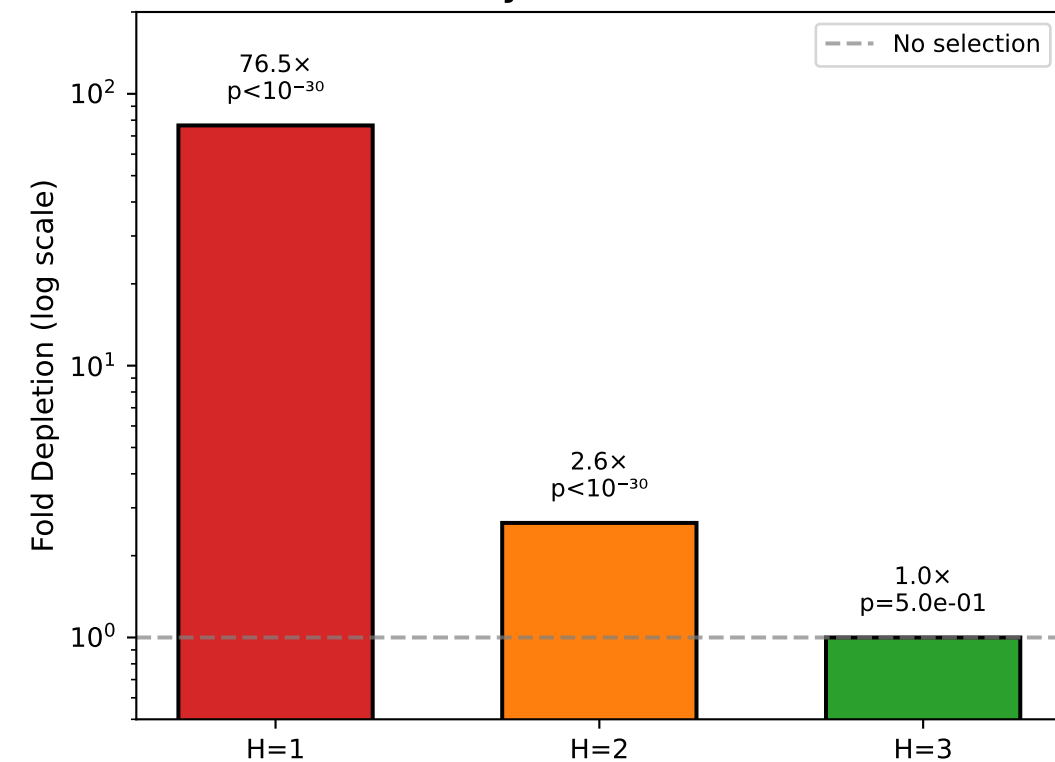
A. Survival Rate by Hamming Distance

B. AP1 Score Distribution by Variant Class

C. Selection Intensity

KEY FINDING

The Selection Paradox

▶ **FORBIDDEN: Only 1 of 31,174 possible H=1 variants observed**

▶ **SIMILAR IMPACT: H=1 AP1 scores ≈ H=2/H=3 scores**

▶ **TARGET: Selection purges site COMPLETION, not binding STRENGTH**

▶ **INTENSITY: 76.5× depletion (p < 10⁻³⁰)**

Interpretation: Human genomes are actively maintained one mutation away from functional AP1 sites.