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Abstract

Proteins are dynamic systems, and understanding dynamics is critical for fully understanding protein function. Therefore, the question of whether laboratory engineering has an impact on protein dynamics is of general interest. Here, we demonstrate that two homologous, naturally evolved enzymes with high degrees of structural and functional conservation also exhibit conserved dynamics. Their similar set of slow timescale dynamics is highly restricted, consistent with evolutionary conservation of a functionally important feature. However, we also show that dynamics of a laboratory-engineered chimeric enzyme obtained by recombination of the two homologs exhibits striking difference on the millisecond timescale, despite function and high-resolution crystal structure (1.05 Å) being conserved. The laboratory-engineered chimera is thus functionally tolerant to modified dynamics on the timescale of catalytic turnover. Tolerance to dynamic variation implies that maintenance of native-like protein dynamics may not be required when engineering functional proteins.