Mutation Fitness Effects Across Populations and Proteins

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The distribution of fitness effects (DFE) among new mutations quantifies how likely a mutation is to have severe, moderate, or minor effect. The DFE is a key determinant of how functional genetic variation is distributed among and within populations, and much research has focused on inferring the DFE from population genetic data. Here, we extend the conventional one-dimensional DFE to address two novel questions. First, how similar are the fitness effects of the same mutation in different populations? To answer this question, we inferred the joint DFE between African and European populations of both humans and Drosophila. We found that similarity varied dramatically among biological processes, pointing toward those processes with the greatest interactions between mutation fitness effects and the environment. Second, how similar are the fitness effects of different mutations at the same protein site? To answer this question, we developed a novel approach to modeling triallelic loci. Applying our approach to Drosophila population genetic data, we found remarkable agreement with biochemical experiments in multiple organisms, suggesting that this similarity is a fundamental property of protein evolution.

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