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ON THE (UN-)PREDICTABILITY OF A FITNESS LANDSCAPE

Since first proposed by Sewall Wright in 1932, the idea of a fitness landscape that relates genotype (or phenotype) to the reproductive success of an individual has fascinated evolutionary biologists and mathematicians alike. The shape of a fitness landscape carries information on the repeatability and predictability of evolution, on the potential for adaptation, the importance of genetic drift, on the likelihood of convergent and parallel evolution, and on the degree of optimization that is (theoretically) achievable. Here, I present a large and complete multi-allelic intragenic fitness landscape of 640 systematically engineered mutations in yeast Hsp90. Through application of a combination of traditional and recently proposed theoretical approaches, we study the accessibility of the global fitness peak, the expected shape of adaptive walks, and the potential for predictability of the fitness landscape topology. We report local ruggedness of the landscape and the existence of epistatic hotspot mutations, and discuss the potential for extrapolation beyond sampled regions of a landscape.