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Hidden Randomness between Fitness Landscapes Limits Reverse Evolution LONGZHI TAN, STEPHEN SERENE, HUI XIAO CHAO, JEFF GORE, Massachusetts Institute of Technology — Natural populations must constantly adapt to the ever-changing environment. A fundamental question in evolutionary biology is whether adaptations can be reversed by returning the population to its ancestral environment. Traditionally, reverse evolution is defined as restoring an ancestral phenotype (physical characteristics such as body size), and the classic Dollo's Law has hypothesized the impossibility of reversing complex adaptations. However, this "law" remains ambiguous unless reverse evolution can be studied at the level of genotypes (the underlying genome sequence). We measured the fitness landscapes of a bacterial antibiotic-resistance gene and analyzed the reversibility of evolution as a global, statistical feature of the landscapes. In both experiments and simulations, we find that an adaptation's reversibility declines as the number of mutations it involves increases, suggesting a probabilistic form of Dollo's Law at the molecular level. We also show computationally that slowly switching between environments facilitates reverse evolution in small populations, where clonal interference is negligible or moderate. This is an analogy to thermodynamics, where the reversibility of a physical process is maximized when conditions are modified infinitely slowly.

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