



CoCo Seminar Series Spring 2016

CoCo/EvoS Joint Seminar:

Greed, Speed, and Deception in the Evolution of Drug Resistance in Malaria

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Academic Building A (AA) G008



The study of empirical fitness landscapes has revealed much about how epistasis crafts the constraints and directionality underlying protein evolution. A common assumption of prior studies is that short sighted, "greedy" evolution creates preferred paths towards absolute fitness peaks, often to the exclusion of alternative, or "less greedy" paths. Absent from these studies are measures of the speed of certain trajectories relative to others, or the possibility for the simultaneous traversal of multiple paths across a single landscape. In this work, we develop and apply a discrete population model to simulate explore rates of adaptation across empirical fitness landscapes for antimicrobial resistance in two species of malaria under various drug treatments. When starting from a single seed genotype, we show that the relative rates of adaptation along accessible trajectories are governed by two forms of clonal interference: (i) within-path competition, which we quantify with a new metric that is remarkably predictive ($R^2 > 99\%$), and (ii) between-path competition, which can be quantified by the amount of deviation from the expected adaptation time predicted by within-path competition. Our findings reveal a non-intuitive and previously unnoticed peculiarity of evolution: specifically, the rate of adaptation along the greediest path in a fitness landscape can be significantly slower than along a less greedy path, with the result that a less greedy path can sometimes lead to a fitness peak more quickly, or by-pass a suboptimal peak on the greedy path. We also investigate deceptiveness in polymorphic populations on these empirical fitness landscapes. The concept of 'deception' in fitness landscapes was introduced in the genetic algorithm (GA) literature to characterize problems where sign epistasis can mislead a GA away from the global optimum. However, existing definitions of deception are categorical and were developed to characterize landscapes independent of population distributions on the landscape. Here we propose two metrics that quantify different aspects of deception as continuous functions of the locations of replicators on a given landscape. We demonstrate varying levels of deception in malarial evolution, and show that the proposed metrics of deception are predictive of some important aspects of evolutionary dynamics. In addition to providing new insights regarding the rate of adaptation, we also discuss how our findings have some practical implications for the application of empirical fitness landscapes toward the goal of subverting the evolution of antimicrobial resistance.

Dr. Margaret (Maggie) Eppstein is Professor and Chair of Computer Science at the University of Vermont. Her research interests include computational modeling and analysis of complex systems in biological, environmental, sociological, and technological domains.

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