Abstract Submitted
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Evolution of antibiotic resistance on a mesa-shaped fitness landscape[1] RUTGER HERMSEN, TERENCE HWA, Center for Theoretical Biological Physics — Rapid emergence of drug resistance is one of the biggest problems facing treatment of diseases ranging from bacterial infection to cancer. Recently it was found that, due to a novel growth-mediated positive feedback mechanism, the growth rate of bacteria exposed to sub-lethal antibiotic levels can drop abruptly when the drug level exceeds a sharp threshold (c.f. the preceding talk by Barrett Deris). This threshold level depends on the degree of expression and activity of the protein(s) providing antibiotic resistance. In environments with spatially varying antibiotic concentrations, this dependence gives rise to a mesa-shaped fitness landscape which provides a strong selective pressure for increasing the expression/activity of drug resistance near the cliff in the landscape. We have performed theoretical studies of evolution on such mesa-shaped fitness landscapes. These studies indicate a high rate of adaptation along the fitness cliff, often exceeding that of evolution on smooth fitness landscapes. The results of these studies establish a dynamic mechanism of evolution driven by a fitness cliff and environmental variability, and are conceptually distinct from the classical Darwinian notion of climbing a fitness gradient.

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