Abstract Submitted
for the MAR14 Meeting of
The American Physical Society

The Structure of Fitness Landscapes in Antibiotic-Resistant Bacteria BARRETT DERIS, Department of Physics, MIT, MINSU KIM, Department of Physics, Emory University, ZHONGGE ZHANG, Division of Biological Sciences, UC San Diego, HIROYUKI OKANO, Department of Physics, UC San Diego, RUTGER HERMSEN, Department of Biology, Utrecht University, JEFF GORE, Department of Physics, MIT, TERENCE HWA, Department of Physics, UC San Diego — To predict the emergence of antibiotic resistance, quantitative relations must be established between the fitness of drug-resistant organisms and the molecular mechanisms conferring resistance. We have investigated E. coli strains expressing resistance to translation-inhibiting antibiotics. We show that resistance expression and drug inhibition are linked in a positive feedback loop arising from an innate, global effect of drug-inhibited growth on gene expression. This feedback leads generically to plateau-shaped fitness landscapes and concomitantly, for strains expressing at least moderate degrees of drug resistance, gives rise to an abrupt drop in growth rates of cultures at threshold drug concentrations. A simple quantitative model of bacterial growth based on this innate feedback accurately predicts experimental observations without ad hoc parameter fitting. We describe how drug-inhibited growth rate and the threshold drug concentration (the minimum inhibitory concentration, or MIC) depend on the few biochemical parameters that characterize the molecular details of growth inhibition and drug resistance (e.g., the drug–target dissociation constant). And finally, we discuss how these parameters can shape fitness landscapes to determine evolutionary dynamics and evolvability.

Barrett Deris
Department of Physics, MIT

Date submitted: 15 Nov 2013

Electronic form version 1.4