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Evolutionary rescue and antibiotic resistance on multicopy plasmids

Abstract: Many bacteria carry extra-chromosomal DNA elements, so-called plasmids, in addition to their chromosome. Plasmids often exist in multiple copies within a single bacterial cell. The copy number has consequences for the dynamics of mutations in plasmid-carried genes, which has recently started to gain increased attention, mainly driven by experimental work. We set up a mathematical model to disentangle the various, partially antagonistic effects of the plasmid copy number on bacterial adaptation if adaptation relies on mutations on multicopy plasmids. Using multitype branching processes, we determine how the plasmid copy number affects the probability of evolutionary rescue for various dominance relationships between the wildtype and the mutant plasmid. We finally focus on the evolution of antibiotic resistance as an instance of undesired rescue and briefly discuss how the antibiotic concentration may influence the dominance function and hence the plasmid copy number that maximizes the risk of resistance. (This is a joint work with Mario Santer)