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The spatial and metabolic profiles of microbial populations non-monotonically impact the growth of antibiotic resistant mutants
KARISHMA KAUSHIK, NALIN RATNAYEKE, Univ of Texas, Austin, PARAG KATIRA, Univ of Texas, Austin. Present address: Columbia University, New York , VERNITA GORDON , Univ of Texas, Austin — Spatial heterogeneity in the distribution of antibiotic is known to accelerate the development of genetic antibiotic resistance. However, the effect of the structure of the microbial population is less well studied. Microbial population structure is a type of spatial structure defined by composition, cell density, and spatial organization of cell types. As our cell types, we use antibiotic-resistant and antibiotic-susceptible (wild-type) *Pseudomonas aeruginosa* along with *S. aureus* and *B. cepacia*, both co-pathogens with *P. aeruginosa*. In spatially-mixed systems, composed of wild-type cells and antibiotic-resistant mutants, we find that increasing cell density reduces the probability of antibiotic-resistant mutant survival in the presence of antibiotic. Using spatially-structured systems, we show that inhibition is mediated by a low-molecular weight, universal, alkaline by-product of bacterial catabolism of amino acids. We demonstrate that for organisms capable of growing on either amino acids or sugars, the nutrient environment provides a switch to activate or de-activate inhibition. Finally, we show that small spatial fluctuations in initial population density can shield mutants from the combined effect of antibiotic and the inhibitory factor

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