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EVOLUTION OF RESISTANCE IN MULTI-DRUG SPACE

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The emergence of resistance during multi-drug chemotherapy impedes the treatment of many human diseases, including malaria, TB, HIV, and cancer. While certain combination therapies have long been known to be more effective in curing patients than single drugs, the impact of such treatments on the evolution of drug resistance is unclear. In particular, very little is known about how the evolution of resistance is affected by the nature of the interactions—synergy or antagonism—between the drugs. I will describe a combined theoretical-experimental approach to study the effect of antibiotic combinations on the evolution of resistance in bacteria. Our results indicate that synergistic drug pairs, typically preferred in clinical settings, actually accelerate bacterial adaptation. Drug antagonism, on the other hand, can generate selection against resistant bacteria, thereby slowing down the evolution of resistance. These results suggest a tradeoff in drug-combination therapy between immediate inhibition of growth and long-term inhibition of resistance.