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Maximum entropy principle for predicting response to multiple-drug exposure in bacteria and human cancer cells KEVIN WOOD, SATOSHI NISHIDA, Harvard University, EDUARDO SONTAG, Rutgers University, PHILIPPE CLUZEL, Harvard University — Drugs are commonly used in combinations larger than two for treating infectious disease. However, it is generally impossible to infer the net effect of a multi-drug combination on cell growth directly from the effects of individual drugs. We combined experiments with maximum entropy methods to develop a mechanism-independent framework for calculating the response of both bacteria and human cancer cells to a large variety of drug combinations comprised of anti-microbial or anti-cancer drugs. We experimentally show that the cellular responses to drug pairs are sufficient to infer the effects of larger drug combinations in gram negative bacteria, *Escherichia coli*, gram positive bacteria, *Staphylococcus aureus*, and also human breast cancer and melanoma cell lines. Remarkably, the accurate predictions of this framework suggest that the multi-drug response obeys statistical rather than chemical laws for combinations larger than two. Consequently, these findings offer a new strategy for the rational design of therapies using large drug combinations.

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