Using Machine Learning to Discover Novel Drug Combinations Against Malaria

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Malaria is a life-threatening disease, caused by plasmodium parasites, that affects nearly half of the world's population, particularly in Africa, where Plasmodium falciparum is the most common and lethal strain. The parasite's mutating nature makes single-drug therapies ineffective as it quickly develops resistance. Combining drugs has proven more efficient and reliable, but screening all possible combinations in the lab is not feasible due to the large combinatorial search space of drugs. To solve this problem, we developed a fully computational method to discover synergistic drug combinations by filtering the search space based on drug activity and toxicity classification models and predicting synergy with regression models. These models were trained and evaluated using publicly available datasets and applied to drugs in Phase III clinical trials and FDA-approved drugs. The classification models obtained high accuracies of up to 85.59 for activity and 86.73 for toxicity. However, the regression models for synergy performed poorly, with the best-performing model obtaining a Pearson R score of only 0.39. Although our study failed to predict synergy accurately, it demonstrated the possibility of reducing the search space of drugs and highlighted the need for further improvements to public datasets and models to discover novel drug combinations against malaria.