Perspective

Be Prepared For the Frequency of Drug Side Effects

Santosh Kumar[*]

Department of Pharmacology, Istanbul University, Istanbul, Turkey

DESCRIPTION

The identification of human side effect frequencies is an essential component of drug risk-benefit analysis. In clinical trials that are randomized and controlled, frequencies are currently determined experimentally. A machine learning framework for computationally predicting drug side effect frequencies is presented by us. Reproducible and biologically interpretable latent drug and side effect signatures are uncovered by our matrix decomposition algorithm [1]. We demonstrate that our method works on 994 side effects and 759 structurally and therapeutically distinct drugs from all human physiological systems. Any drug for which a small number of side effect frequencies have been identified can be used with our method to predict the frequencies of additional side effects that have not yet been identified. We demonstrate that the biology underlying drug activity can be learned from our model: The distinct anatomical categories of the drugs and the distinct routes of administration of the drugs are linked to specific components of the drug signatures [2].

In drug risk–benefit analysis, estimating the frequency of side effects is crucial. Currently, in randomized controlled trials, these frequencies are estimated using the intervention and placebo groups. In clinical medicine, these trials are the standard method for preventing selection bias despite their limitations in terms of sample size, time frame, and lack of accrual.

However, it is common knowledge that many adverse effects are not discovered during clinical trials but are discovered after the drug has been released to the general public. As a result, drug side effects continue to be a major cause of healthcare-related morbidity and mortality, costing billions of dollars annually. For the purpose of anticipating a drug's adverse effects, a number of computational strategies have been proposed [3]. However, these techniques are only able to predict the presence or absence of a drug side effect and not its frequency, so their application to drug risk–benefit analysis is limited.

In clinical practice, accurate estimation of side effect frequency is critical to patient care, but pharmaceutical companies also need it because it reduces the risk of drug withdrawal or costly reevaluation of side effect frequency in new clinical trials.

A machine learning strategy for predicting the frequency of drug side effects is presented here. We demonstrate that our method works well with drugs from various therapeutic classes and side effects from all physiological systems. Our method can predict the frequency of a wider range of unknown side effects based on a small number of experimentally determined effects [4]. This is, to our knowledge, the first computational approach to the issue of predicting the frequency of drug side effects. Computational predictions can serve as complementary hypotheses in the early stages of clinical trials to guide risk assessment in subsequent phases, which is an important application of our method. A matrix decomposition algorithm that learns a small set of latent features (or signatures) that encode the biological interaction between drugs and side effects is our method for predicting the frequency of drug side effects. Movie recommendation systems, which offer users movie recommendations, serve as inspiration for our model: Drug side effects are recommended by our recommendation system. Most importantly, our matrix decomposition must not be negative; The benefits of this include making the parts-based representation explicit and providing biological interpretability [5].

To put it another way, drugs have a set of learned non-negative characteristics that, when added together, account for the frequency of side effects across the entire drug repertoire. As a result, our predictions can be explained, and each feature can be understood in terms of how drugs affect particular human physiological systems. In addition, we demonstrate that these characteristics capture shared drug clinical activity, drug targets, and the anatomy/physiology of side effect phenotypes in relation to various routes of administration.

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