Machine learning helps finding new targeted therapies

Title of the dissertation
Machine learning for systems pharmacology

Contents of the dissertation
Most of the currently used drugs are small-molecule compounds that achieve their therapeutic effects through interacting with other molecules, especially proteins, in the human body. Some of these drug-target interactions can also help identifying new uses of existing drugs, in the process called drug repurposing, whereas other interactions can cause harmful side effects. However, despite the recent technological advances, the determination of all drug-protein interactions in the laboratory is still difficult in practice. The design of new drugs and therapies is further complicated by the difficulty in pinpointing the key proteins involved in complex diseases, such as cancer or schizophrenia, that should be targeted by a drug in order to achieve a maximal therapeutic effect. Moreover, both efficacy and safety of a drug depend on the genomic background of an individual patient.

This thesis proposes machine learning frameworks that support experimental efforts of finding new drugs and therapies. In particular, one of the main contributions lies in the development of a method that facilitates the identification of the contribution of the variation in a DNA sequence of individuals to their risk of developing diseases, towards prioritisation of potential therapeutic targets for the disease. The other class of the machine learning methods developed in this thesis enables the prediction of responses of patients with different genomic backgrounds to drug therapy, as well as prediction of new drug-protein interactions. As a specific example, we predicted and validated in the laboratory four new protein targets for an investigational kidney cancer drug tivozanib, which could point researchers to its potential novel uses and repositioning opportunities.

Field of the dissertation
Computer Science

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