Prediction of drug effect using AI in the context of computational drug repositioning

Supervision:

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Localisation :

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Context:

AIstroSight develops digital approaches to facilitate the discovery of treatments for rare diseases affecting the brain using a range of complementary methods including biophysical modeling, computer simulations, machine learning and AI. To study these diseases, AIstroSight adopts a multiscale viewpoint, from the whole organ (brain imaging) down to the molecular level (omics and signaling data). In terms of drug discovery strategy, we explore several approaches and one of them is drug repositioning.

The concept of repositioning (or repurposing) is the following: take an existing drug, validated against a given disease, and determine whether it can be used to treat diseases other than the one for which it is already used. Computational drug repositioning consists in using in silico approaches to find new indications for an existing drug [1]. These approaches are usually empowered by the exploitation of large databases related to the effects of drugs. Many open access public databases are available that contain information about drugs [2], their effects at the molecular level [3] and on the body/pathologies [4].

One of AIstroSight objectives is to develop resilient methods that are generalizing enough so as to be applied for different diseases without having to completely rethink them each time. In this perspective, machine learning and AI seems most suited to the problem of drug repositioning: their ability to integrate large amounts of multimodal data makes it possible to solve complex problems with the only limit being the volume and diversity of the data used for their training.

Internship objectives :

The objective of this internship is to develop and evaluate a proof-of-concept for an in silico drug repositioning system using information extracted from open public databases. The method will be based on a Deep-Learning approach loosely inspired by Zeng et al [5]. Databases of drugs will be encoded into networks on the basis of

e.g., the similarity between the effects of drugs on gene expression or the molecular targets of the drugs. Graph embedding technics (more precisely node embedding) will then be used to build a low-dimensional vectorial representation of the nodes preserving the local topology of the networks (i.e., “similar” drugs in the graph are closed points in the vectorial space). This embedding will be passed through a final classification network to learn the pathology(ies) treated by a node/drug. An additional step could be to use an auto-encoder stage after graph embedding to generate a lower-dimensional and more coherent latent space representation on which classification will be based.

The intern will develop this drug repositioning system and evaluate it under the direction of the supervision team. The internship will take place within the premises of the Inria research center, on La Doua Campus (north of Lyon).

Expected skills:

- Basic knowledge of how machine/deep learning models work and how to train them
- Good programming skill in Python
- Adaptation to the encountered problems
- Communication about their work and results
- Interest in biological and medical applications

To apply :

Send your CV and a cover letter to the following email adress (nicolas.simon@inria.fr) and CC this 2 email adresses (hugues.berry@inria.fr and thomas.guyet@inria.fr).

References :

[1] Park, K (2019) Transl Clin Pharmacol, https://tcpharm.org/DOIx.php?id=10.12793/tcp.2019.27.2.59
[2] https://pubchem.ncbi.nlm.nih.gov/
[3] https://lincsproject.org/LINCS/
[4] https://go.drugbank.com/
[5] Zeng et al. (2020) Chem Sci, https://doi.org/10.1039/C9SC04336E