AtomNet: Artificial Intelligence for Drug Discovery

Nina Versin

Introduction

First developed at the Computational Biology group of the university of Toronto, AtomNet is a deep convolutional neural network used for drug discovery with unseen speed and precision. AtomNet is able to predict the bioactivity of small molecules, even predicting new active molecules for previously undrugged targets .

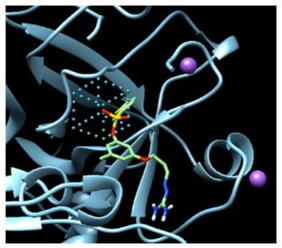
Idea

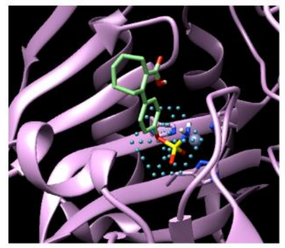
The optimal drug candidate is both safe and effective. The best optimization tool for binding prediction was a multi-task deep neural network. Ligand-based techniques can however only be used for targets with a lot of previous data available. This is why AtomNet adds structural information for better performance.

Method

- Biochemical interactions are local effects and defined by the spatial arrangement and bonding of proximate atoms.
- Convolutional networks hierarchically combine these local features into more complex models of the distant effects of biochemical interactions
- A protein-ligand pair is represented by a 3D voxel containing channels for the atom types. These voxels are used as input to the network.
- The complete network consists of the input layer, four convolutional, two fully-connected layers and a cost function containing the probabilities of the molecules being (in)active.
    - AtomNet then autonomously learns the features present in molecular binding.

Results





- AtomNet achieves a large margin of improvement in accuracy over previously established methods.
- The accuracy of AtomNet is comparable to wet lab experiments, only much faster, being able to screen millions of compounds each day.
- Arbitrary molecular features can be discovered by the model and the spatial arrangement of input atom types can be inferred without any chemical prior knowledge.
- Screening time is much less than with conventional methods and has the possibility to significantly decrease the time-to-discovery of new treatments.

Conclusion

With the addition of structural information to ligand-based techniques, favorable and unfavorable interactions between ligands and targets can be found, even if none were previously known for that target. Predicting molecular binding fast can reduce time-to-discovery, eliminate toxic molecules early in the process and screen for even the most difficult targets.
Since the publication of this research, the company AtomWise was founded, using the AtomNet technology for drug discovery. Some of their most notable examples include new treatments for the Ebola virus and Multiple Sclerosis.

References

Wallach I., Dzamba M., and Heifets A. Atomnet: A deep convolutional neural network for bioactivity prediction in structure-based drug discovery. CoRR, abs/1510.02855, 2015.