ORT_04 - Development of a decision tree to predict correct poses of PD-1/antibody complexes obtained by docking

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Introduction: Cancer is a serious health problem. Research has shown that only in 2020 it caused about 10 million deaths and 19.3 million cases. Cancer cells develop due to mutations in proto-oncogene and/or tumour suppressor genes. It is worth mentioning that one of the characteristics of cancer cells is to prevent their elimination by escaping the immune system through the activation of negative regulatory pathways, also known as immune checkpoints. In this work, the PD-1/PD-L1 pathway is highlighted.
Currently, one of the most effective treatments is based on the use of monoclonal antibodies (mAbs) as inhibitors of immunological checkpoints.
The application of bioinformatics tools in the pharmaceutical industry has enabled the process of research and development of new drugs to be faster, more effective, and less costly. Some of these bioinformatics approaches include molecular modelling, molecular docking, and molecular dynamics simulation. However, accurate identification of correct poses is still an issue.

Objective: This work aims to build a decision tree for the correct identification of new viable PD-1/antibody complexes, based on redocking of crystallographic structures containing PD-1.

Methodology: Based on algorithms, machine learning techniques allow us to build a machine in which it can make is own decisions and provide a result to the user. A machine learning approach highlighted in this work is decision tree, a powerful statistical tool used for classification, prediction, interpretation of a data system based on multiple covariates guided by data training.

Results: Thus, the decision tree was developed through Haddock's output parameters: HADDOCK score; Cluster size and RMSD, which were obtained during redocking of approximately 23 crystallographic structures of PD-1 complexed with its ligands deposited in the PDB repository. At least one correct and nine incorrect poses, respectively, were recovered from each complex. We show that our developed decision tree shows accuracy over 85%, minimizing the risk of selecting unstable pose as the correct one.

Conclusion: The decision tree will be used to define whether the complexes formed during docking are satisfactory or not.

Keywords: Antibody; Decision tree; PD-1