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GPCR_LigandClassify.py; a rigorous machine learning classifier for GPCR targeting compounds

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The current study describes the construction of various ligand-based machine learning models to be used for drug-repurposing against the family of G-Protein Coupled Receptors (GPCRs). In building these models, we collected > 500,000 data points, encompassing experimentally measured molecular association data of > 160,000 unique ligands against > 250 GPCRs. These data points were retrieved from the GPCR-Ligand Association (GLASS) database. We have used diverse molecular featurization methods to describe the input molecules. Multiple supervised ML algorithms were developed, tested and compared for their accuracy, F scores, as well as for their Matthews' correlation coefficient scores (MCC). Our data suggest that combined with molecular fingerprinting, ensemble decision trees and gradient boosted trees ML algorithms are on the accuracy border of the rather sophisticated deep neural nets (DNNs)-based algorithms. On a test dataset, these models displayed an excellent performance, reaching a ~ 90% classification accuracy. Additionally, we showcase a few examples where our models were able to identify interesting connections between known drugs from the Drug-Bank database and members of the GPCR family of receptors. Our findings are in excellent agreement with previously reported experimental observations in the literature. We hope the models presented in here synergize with the currently ongoing interest of applying machine learning modeling in the field of drug repurposing and computational drug discovery in general.

Biography

Barakat received his PhD in biophysics from the University of Alberta in 2012 followed by a postdoctoral fellowship in the lab of the Nobel Laureate, Professor Michael Houghton, for two years. Dr. Barakat joined the Faculty of Pharmacy at the University of Alberta as an assistant professor in 2014. His research stands at the multidisciplinary interface of physics, biology and computer science. His research is focused on understanding the structure-function-relationship of cardiac ion channels in health and disease and on developing and applying state-of-the-art computational drug discovery tools to discover new antiviral and immunotherapeutic small molecule drugs.