

Unraveling regulatory associations using explainable AI

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Explainable AI (XAI) is an active research domain in the machine learning (ML) community. Its application in biological and medical contexts have led to new exciting questions. In particular, local explanations for models offer in-depth insights but require costlier computations than global explanations. Thus recent research has focused on implementing faster algorithms to compute local explanations. SHAP values are a popular local explainability framework that give human-intuitive explanations and have a strong mathematical foundation. In the case of an AI model with a huge number of features, the computation of said SHAP values is computationally costly, and that challenge has led to several approximation methods, including our proposal of an algorithm allowing to dynamically select the top k features: topShap. A typical biological context where AI/ML models have many features is for Gene Regulatory Network (GRN) inference and analysis. GRNs capture regulatory information in the form of Transcription Factor – Target Gene (TF–TG) interactions, and plenty of ad-hoc methods exist to provide answers to questions specific to a study. Our objective instead is to propose a general method that will be useful across a wide range of studies, namely the detection of “marker regulatory associations”, in similar vein as marker genes. In this context, the use of the topShap algorithm makes the computation feasible on modest hardware and compatible with any ML model used for inferring the GRN. Our analysis method is composed of three steps: (i) building regression models that predict a transcription factor expression according to the expression of the target genes, (ii) computing per cell the top-k features using topShap, (iii) detecting marker regulatory associations characteristic of subgroups of cells. We apply this workflow to the classic benchmarking dataset PBMC3k and demonstrate insight through marker regulatory associations complements the standard approach of detection of marker genes.

Acknowledgment This work was partially funded by PEPR Santé Numérique, project 22-PESN-0002; Fondation ARC under grant ARCPJA22020060002212; Institut National du Cancer under grant PLBIO22-071; the National Institutes of Health (NIH) award R01DC020478 and BQR INSA Lyon 2023 Neurinfo.