PhD proposal at the University of Angers : Machine learning for Exploring Subdominance in PolyPLOID Genomes

Research unit : IRHS (Institute of Research in Horticulture and Seeds)

Co-supervision : LAREMA (Department of Mathematics at the University of Angers)

Scientific context :
Whole Genome Duplications (WGD), which are very common in plants, seem to coincide with periods of extinction or global change. Apple underwent a WGD 27 Mya ago (Lallemand et al., 2023), and since footprints of this WGD can still be found in the genomes of modern varieties, the apple tree is an interesting organism for studying the evolution of gene families after WGD (Daccord et al., 2017). From a general perspective, understanding the role of duplicated chromosomes and their contribution to phenotype development is a major challenge in the context of climate change.

Biological questions :

Two duplicated genes are called ohnologs if they are the consequence of a WGD event. In Lallemand et al. (2003), we have shown, thanks to a bioinformatic approach, that there exists an imbalance between ohnolog fragments. Some chromosomal fragments contribute more than their ohnologs to the phenotypic variation. We have named this phenomenon chromosomal subdominance. During this phd, we will tackle the following biological questions:

- Can we confirm and capture this imbalance through genomic prediction, which takes into account allelic variations between individuals?
- Can we take advantage of the knowledge of this imbalance to predict the phenotype more accurately ?

Mathematical questions :

We will also tackle the following mathematical questions:

- Can we consider probability distributions within a neural network, and use them as prior distributions on parameters, in the same way as what is done in mixed model tradionally used by geneticists in genomic prediction ? Such model would lead to a better understanding of the bias of Artificial Intelligence and a better understanding of the decisions made by algorithms. It would also help to improve predictions.

- Can we introduce a genomic version of Random Forests taking into account the genomic covariance between individuals while building classification trees ?

Main steps of the phd:

To begin with, a simulation study will be carried out using the REFPOP apple population (Jung et al, 2020, 2022). The phenotype will be simulated by considering various possible links (additivity, epistasis, dominance, non-linearity ...) between phenotype and genotype at QTLs (QTL = locations of the genome responsible for the variation of quantitative trait). In terms of machine learning, the preferred methods will be Genomic BLUP, random forests, Lasso, Elastic-Net, SVM, RKHS and neural networks. For each simulated trait architecture, we'll extract the best statistical learning method able to capture the imbalance between ohnologs.

In a second step, we will try to improve existing statistical methods in genomic prediction, taking advantage of this imbalance. Given the proximity between mixed models in genomics and in spatial statistics, we will built on recent mathematical results in spatial statistics (Wikle and Zammit-Mangion 2023) to improve existing methods in genomic prediction. For instance, we will focus on neural networks and on random forests. In neural networks, Chen et al. (2021) introduced DeepKriging, a deep neural network where the spatial dependency is modeled by adding an extra layer to approximate the spatial process using a basis of functions. For random forest, Saha et al. (2021) suggested, in order to build a decision tree, to replace the least-squares criterion at each node split by an optimization taking into account the spatial correlation structure induced by a Gaussian process.

In order to be more familiar with these new methods, we will consider their associated packages : RandomForestsGLS (Saha et al., 2021), and the Python code of DeepKriging (https://github.com/aleksada/DeepKriging). We will try to improve Deep Kriging (Chen et al., 2021) and the random forests (Saha et al., 2021), by elaborating new mathematical formulas dedicated to genomics. The goal is to reduce the prediction error, and to quantify the information loss (in terms of prediction accuracy) when the two ohnologs are not included in the prediction model (cf. Rabier and Grusea 2021, in another context).

Skills :
- Statistical learning (Random forest, Neural networks, Lasso ...), high-dimensional data analysis, mixed model
- R or Python
- Evolutionary biology would be a plus

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