Deep learning for genomic prediction and tasks learned on the way

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Introduction and motivation

- Genome enabled prediction of complex traits aims to predict a measurable characteristic of an organism using its genomic information.
- Deep Learning architectures: CNNs, GCNs and CNN+GCN.
- Increasing number of SNPs, increases number of parameters and memory needed very fast.
- Uses of AEs and VAEs in population genomics.
- Python library is in process to be released at github.com/farielberry-lab

Datasets and experiments settings

German Holstein bulls:

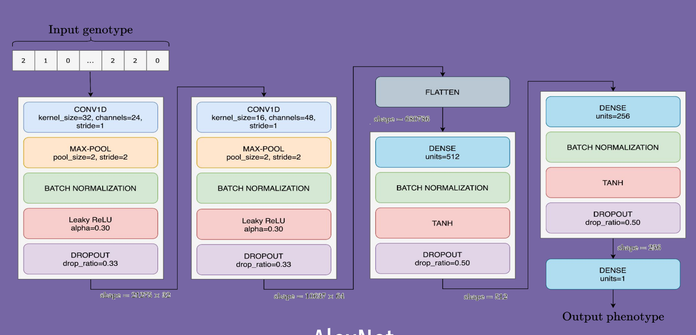
- Individuals (*n*): 5024
- Genotypes (*p*): 42.551 SNPs after quality control filtering.
- Phenotypes: somatic cell score (SCS) and milk yield (MY).
  - SCS is governed by many small effect loci.
  - MY is determined by a few moderate effect loci and many small effect loci
- Experiments were repeated 10x using random splits.\
- Hyperparameter searches and fine tuning: five-fold X-val.

Jersey bulls:

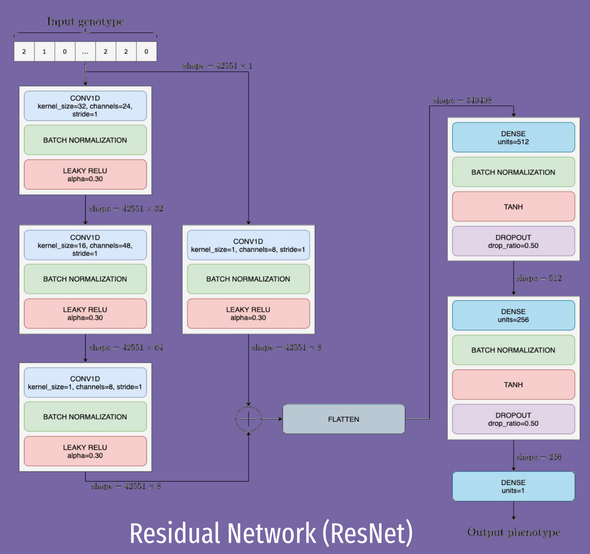
- Individuals (*n*): 1569 (from 2008 to 2018)
- Genotypes (*p*): 95.434 SNPs after quality control filtering.
- Phenotype: Sire Conception Rate (SCR)
  - Expected difference between the conception rate (CR) of a bull compared with the mean of the rest of the population in a certain year. CR: amount of successful inseminations as a fraction of the total inseminations attempted

Convolutional Neural Networks (CNN) + Residual CNN (ResNet)

- CNNs are a classical architecture used in image analysis.
- AlexNet-like CNN, residual CNN, with their corresponding single and multitrait variants were tested.
- The ResNet made the difference in MY prediction.

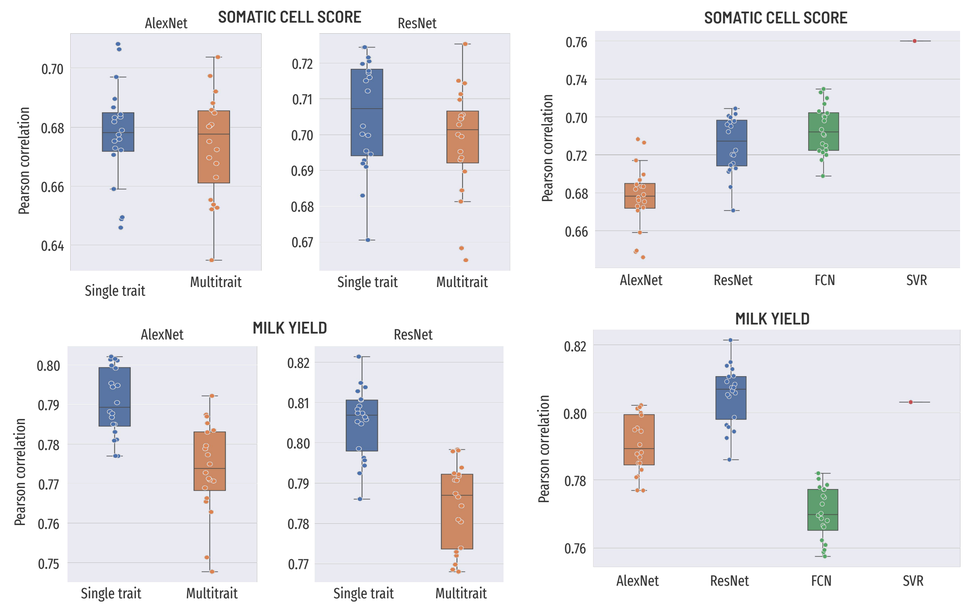


AlexNet

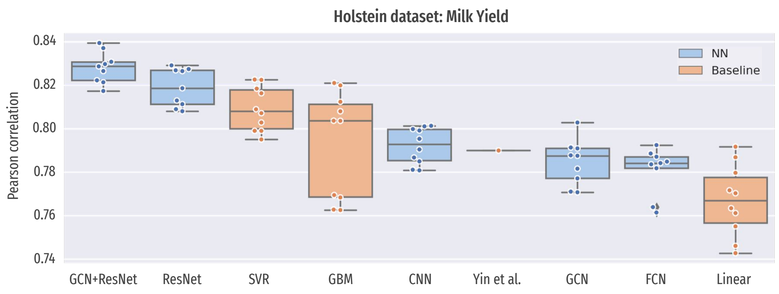


Residual Network (ResNet)

Results Holstein dataset (n: 5000, p: 42k)



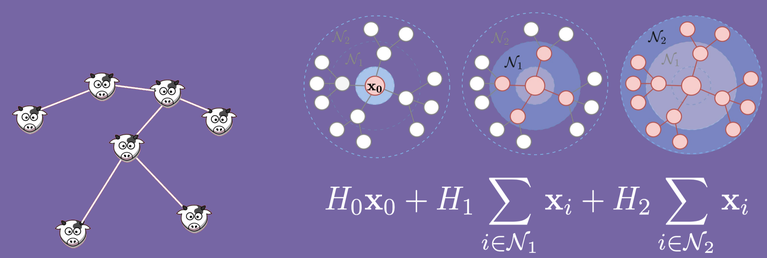
Holstein overall results



- Grid search and fine tuning parameters is crucial. Out of the box methods will not (ever) work.
- Adding information of relatives improves the predictions.
- Number of parameters grows with the model complexity.
- More results on www.comet.ml/dna-i

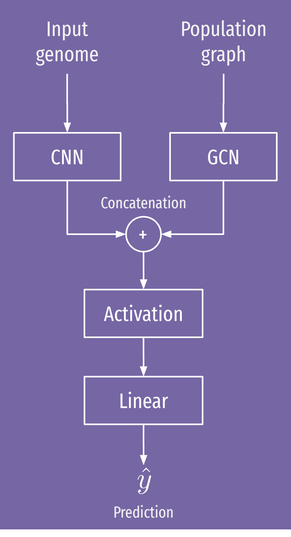
Graph Convolutional Networks (GCN)

- Build a graph with an individual's parameter in nodes and a similarity measure between nodes as edge's weights.
  - CNN output in each node
- *Convolution* supported in the graph for data aggregation.

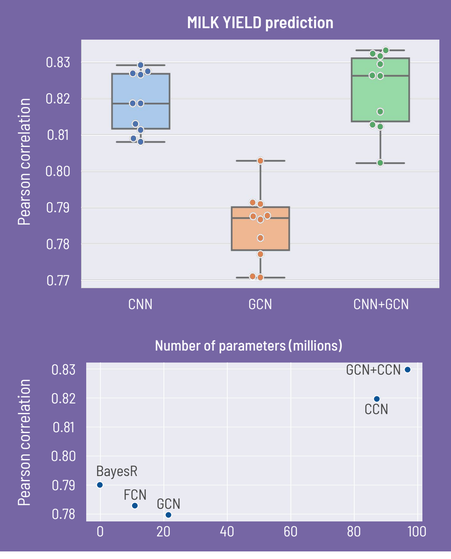


$$H_0\mathbf{x}_0 + H_1 \sum_{i\in\mathcal{N}_1} \mathbf{x}_i + H_2 \sum_{i\in\mathcal{N}_2} \mathbf{x}_i$$

$$H_k \in \mathbb{R}^{d_{\text{in}}\times d_{\text{out}}}$$



Holstein dataset



(Variational) Autoenconders (VAE and AE)

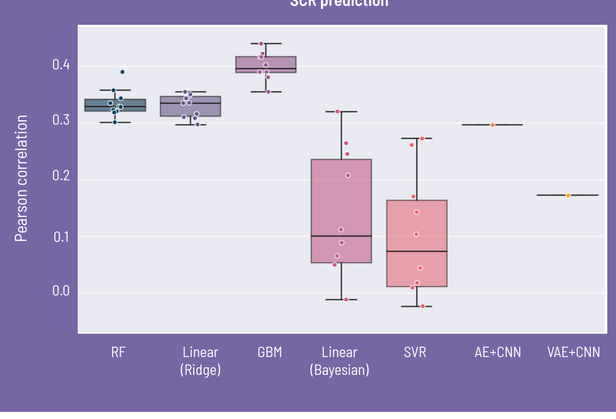
AEs and VAEs are capable of learning dense representations of the input data. They can be used for:

- Dimensionality reduction for visualization or memory reduction through its latent representations.
- Imputation: train the data without missing data, then use the autoencoder on data with missingness.

Algorithm for genomic prediction:

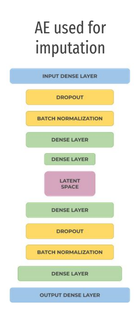
1. Split genotypes by chromosome
2. Fit a dimensionality reduction network (AE, VAE) for each one. The latent dimension is a fixed proportion of the input dimension.
3. Concatenate the latent representations to build the low-dimensional genotype.
4. Train a neural network (eg. CNN) on the low-dimensional genotype for prediction.

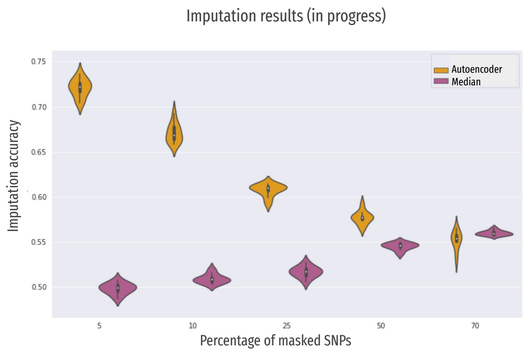
Jersey dataset



Imputation

The AE can be trained including missing data in the data set.





Conclusions and future work

- Same network architectures can be useful for different tasks (imputation, dimensionality reduction).
- Understand how missing data affects the latent representations.
- Good latent representations could overcame imputation.
- As datasets (features and individuals) grow, dimensionality reduction could be as important as regularizations.

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