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agriscience

Learning from data:

Technical Nuances of Machine Learning in Plant Breeding

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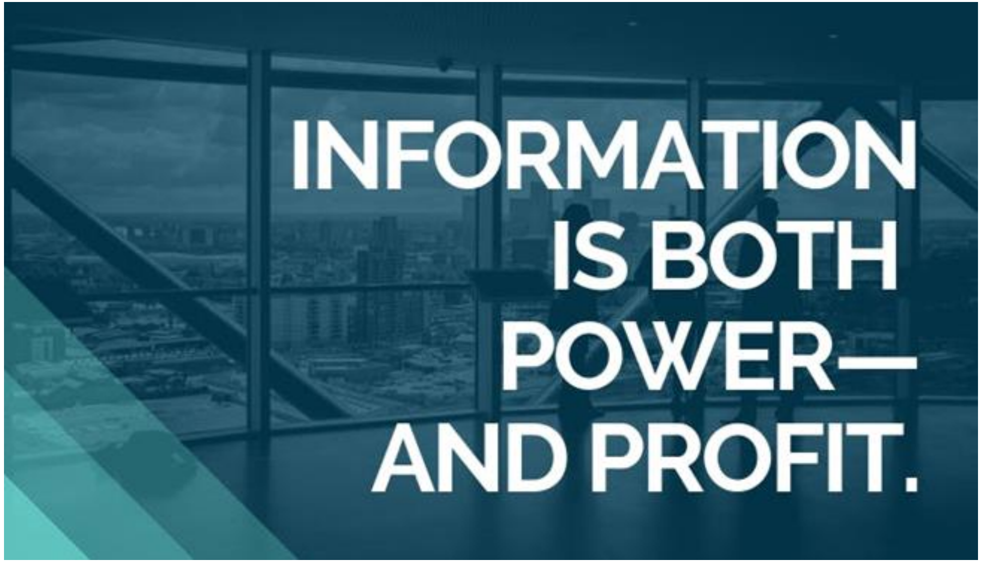
Adequate use of



Outline

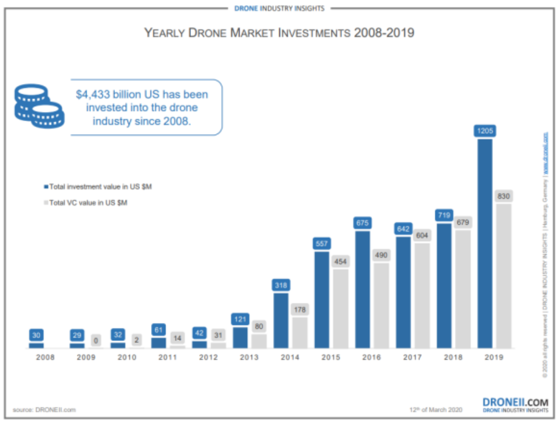
Three faces on machine learning

1. Good
2. Bad
3. Ugly

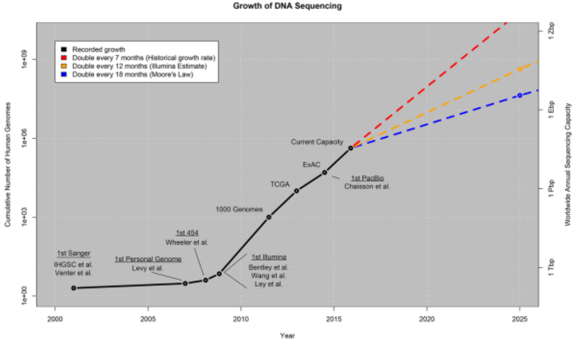
1. **Good**
    - Intro and motivation
    - Filters in PB
2. **Bad**
    - Metrics of success
    - Adequate validation
3. **Ugly**
    - Optimization
    - From RR to NN

Part 1 – Good learners

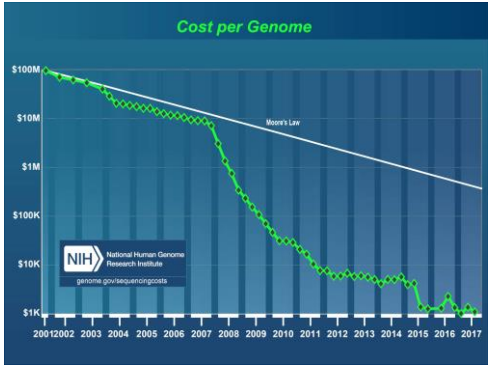
More Pheno



More Geno



The Cost of Sequencing a Human Genome. NIH.
https://www.genome.gov/27565109/the-cost-of-sequencing-a-human-genome/



Stephens, Z. D.et al. (2015). Big data: astronomical or genomical? *PLoS biology*, *13*(7), e1002195.

More Env

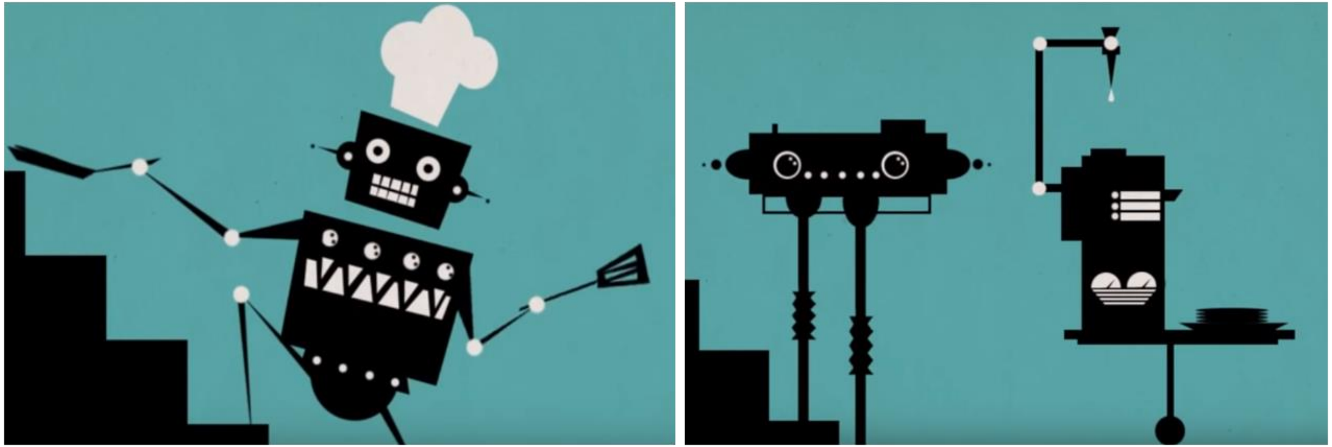
- UC Merced - GridMET
- NWS - NOAA
- NASA - GISS
- Harmonized SoilDB
- USDA - SSURGO

More Computing

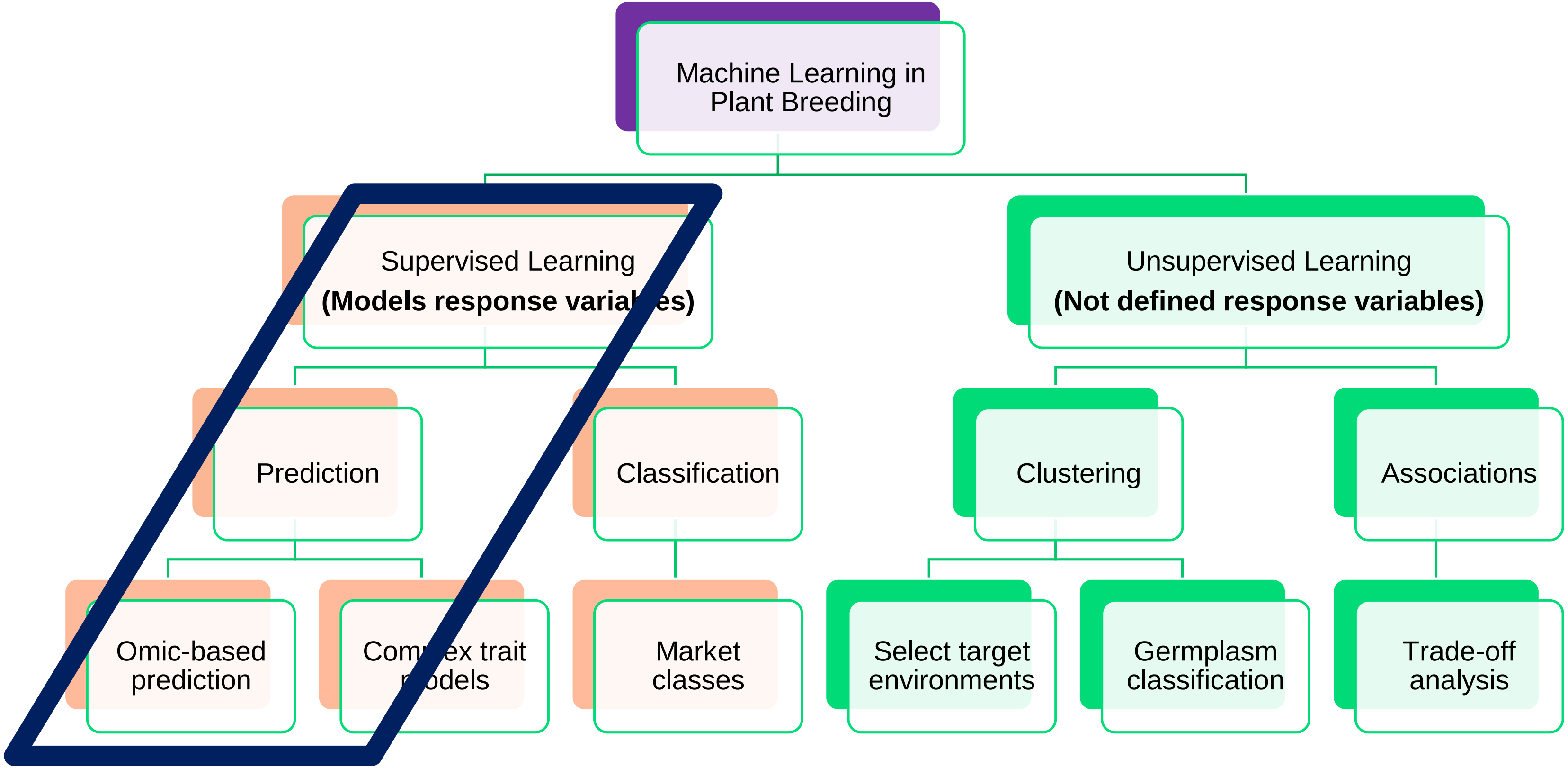
Alencar.Xavier@Corteva.com
Corteva Biostatistics, Methods group

Why is machine learning good for?

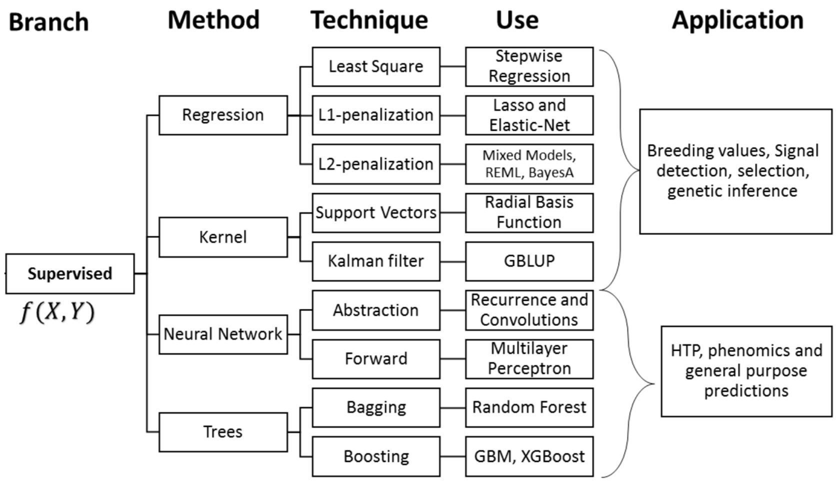
Good for solving **single well-defined problem**



Source: https://www.youtube.com/watch?v=MPR3o6Hnf2g


Machine Learning in Plant Breeding
Supervised Learning
(Models response variables)
Unsupervised Learning
(Not defined response variables)
Prediction
Classification
Clustering
Associations
Omic-based prediction
Complex trait models
Market classes
Select target environments
Germplasm classification
Trade-off analysis

Key of supervised learning: FILTERING



Branch

Method

Technique

Use

Application

Supervised

$f(X,Y)$

Regression

Least Square

Stepwise Regression

L1-penalization

Lasso and Elastic-Net

L2-penalization

Mixed Models, REML, BayesA

Kernel

Support Vectors

Radial Basis Function

Kalman filter

GBLUP

Breeding values, Signal detection, selection, genetic inference

Neural Network

Abstraction

Recurrence and Convolutions

Forward

Multilayer Perceptron

Trees

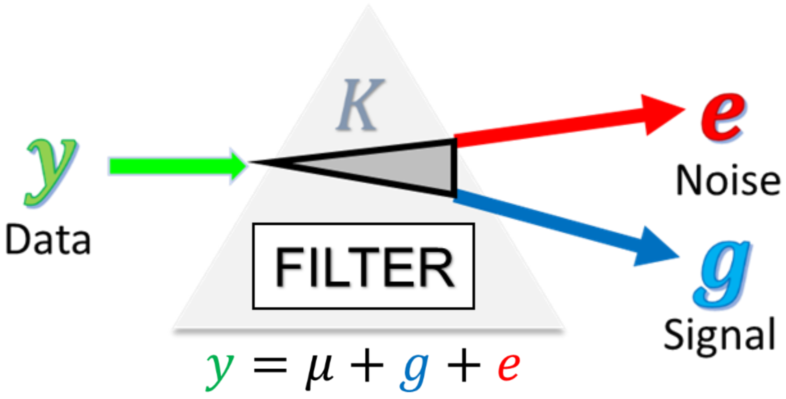
Bagging

Random Forest

Boosting

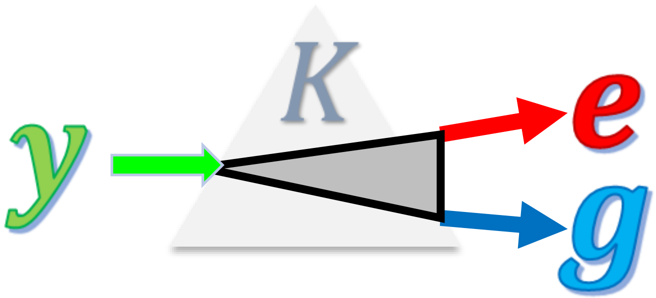
GBM, XGBoost

HTP, phenomics and general purpose predictions

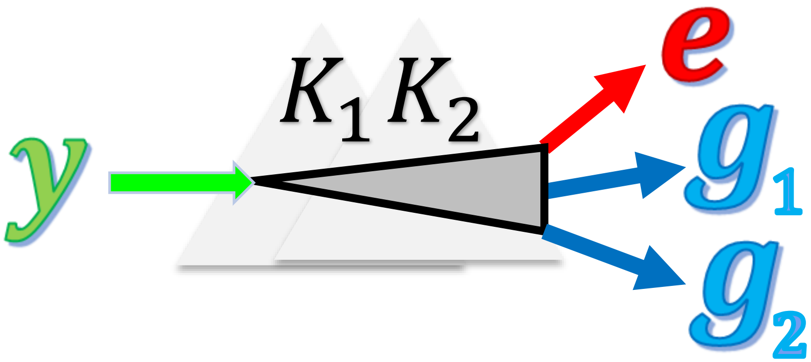


$$y = \mu + g + e$$

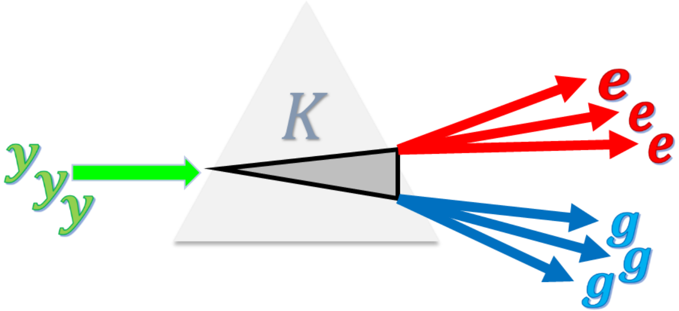
Generalizations of simple filters



1) Multiple filters

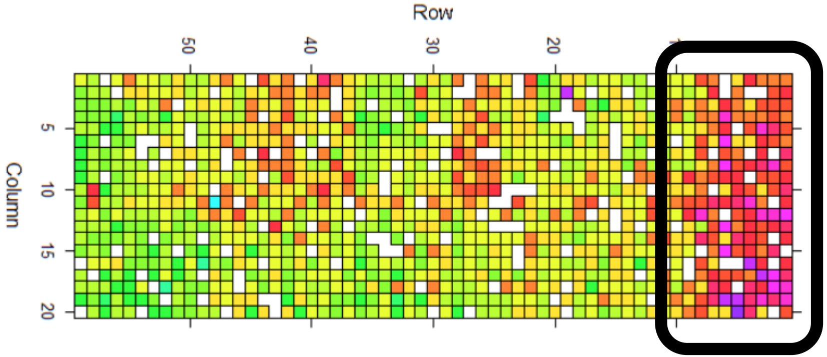


2) Multi-response filters

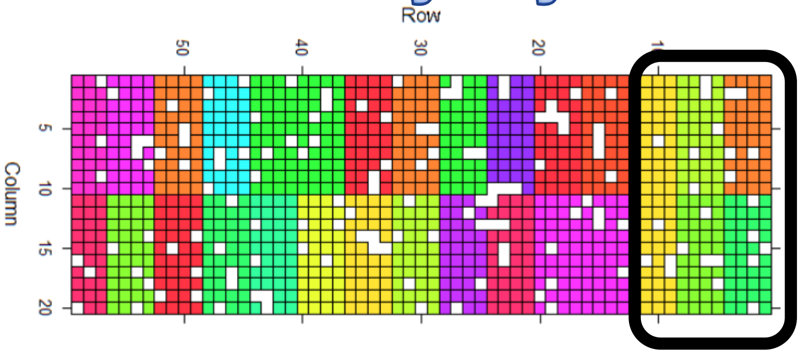


1) When bother with multiple filters?

Field variation

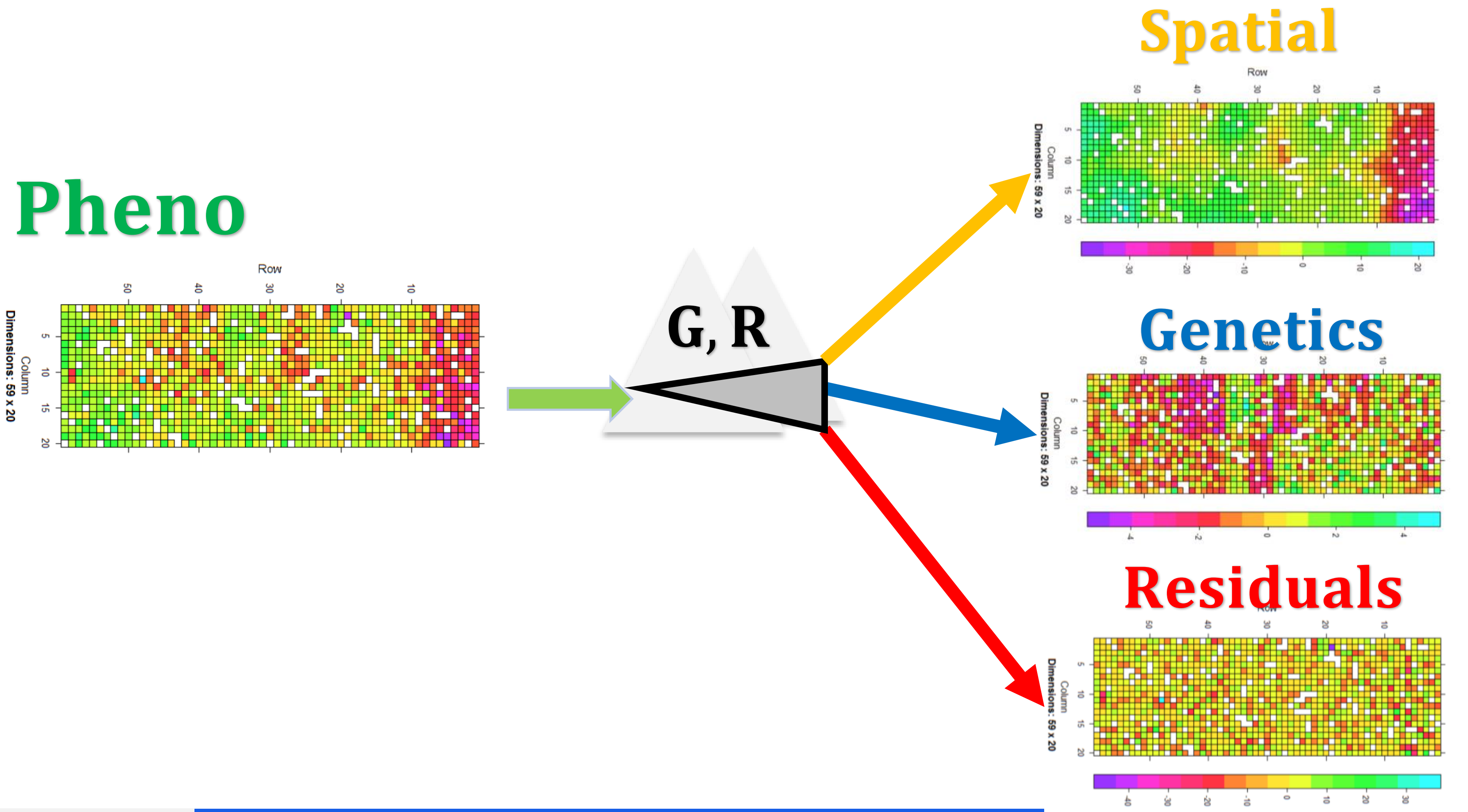


Family layout



Some families were placed on unfavorable side of the field…

SoyNAM field,
Indiana 2014



Pheno

G, R

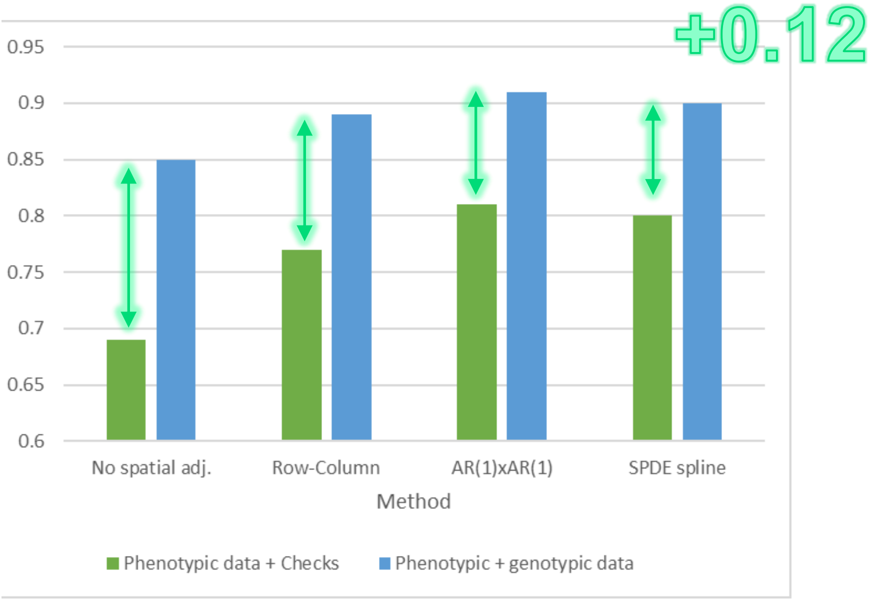
Spatial

Genetics

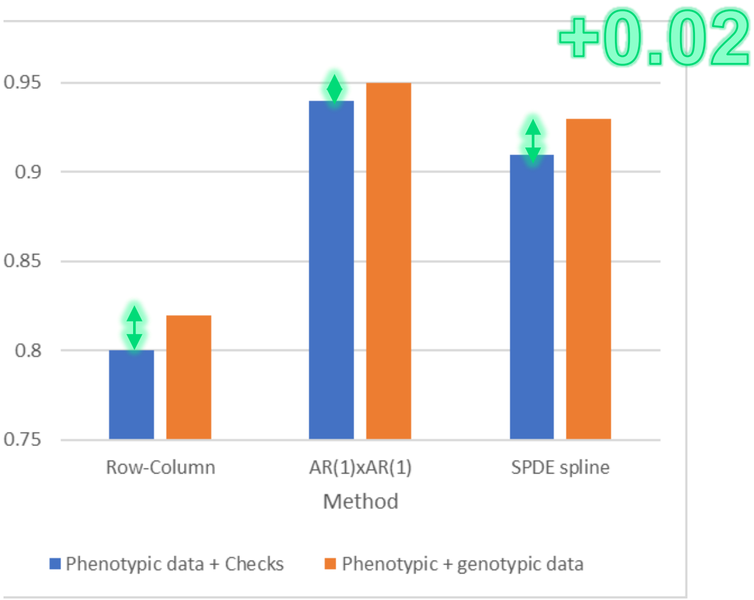
Residuals

Multiple filters benefit separability of signals

Improvement in genetic accuracy



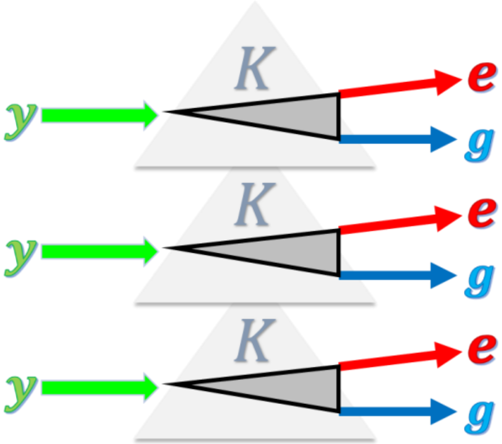
Improvement in spatial accuracy



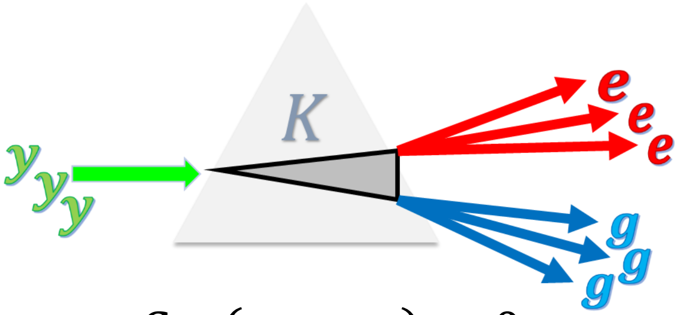
Results derived from simulation of field with1500 plots, 1275 non-replicated entries + checks, from single trials

2) When bother with multi-response filters?

Filter one input at a time
(parallelizable)



Filter passing multiple input at once



$$\mathrm{Cor}(\mathrm{g_A}, \mathrm{g_B},) \neq 0$$

New information

Genetic correlation table

	g_1	g_2	g_3
g_1	1	ρ_{12}	ρ_{13}
g_2	ρ_{21}	1	ρ_{23}
g_3	ρ_{31}	ρ_{32}	1

- **Bivariate model**

Objective gain of information!

$$\begin{bmatrix} y_1 \\ y_2 \end{bmatrix} = \begin{bmatrix} g_1 \\ g_2 \end{bmatrix} + \begin{bmatrix} e_1 \\ e_2 \end{bmatrix}, \qquad y \sim N(0, G \otimes \Sigma_a + I \otimes \Sigma_e)$$

- Model equation

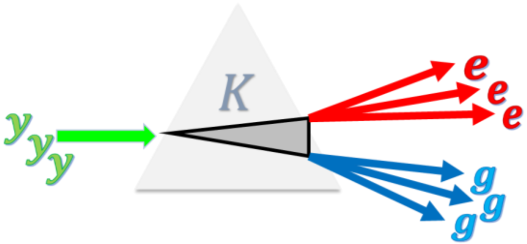
$$\begin{bmatrix} Z_1' \Sigma_e^{11} Z_1 + G^{-1} \Sigma_a^{11} & Z_1' \Sigma_e^{12} Z_2 + G^{-1} \Sigma_a^{12} \\ Z_2' \Sigma_e^{12} Z_1 + G^{-1} \Sigma_a^{12} & Z_2' \Sigma_e^{22} Z_2 + G^{-1} \Sigma_a^{22} \end{bmatrix} \begin{bmatrix} g_1 \\ g_2 \end{bmatrix} = \begin{bmatrix} Z_1' (\Sigma_e^{11} y_1 + \Sigma_e^{12} y_2) \\ Z_2' (\Sigma_e^{22} y_2 + \Sigma_e^{12} y_1) \end{bmatrix}$$

- **Univariate vs bivariate solution for a given predictor**

$$g_1 \quad = (Z_1' \Sigma_e^{11} Z_1 + G^{-1} \Sigma_a^{11})^{-1} (Z_1' \Sigma_e^{11} y_1)$$

$$g_1 | g_2 = (Z_1' \Sigma_e^{11} Z_1 + G^{-1} \Sigma_a^{11})^{-1} (Z_1' (\Sigma_e^{11} y_1 + \overbrace{\Sigma_e^{12} y_2) - (Z_1' \Sigma_e^{12} Z_2 + G^{-1} \Sigma_a^{12}) g_2}^{\text{EXTRA INFORMATION}})$$

Sparse & Directed Filtering



Genetic correlation table

	g_1	g_2	g_3
g_1	1	ρ_{12}	ρ_{13}
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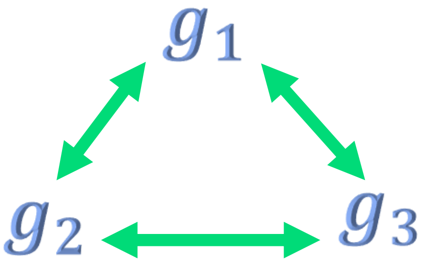
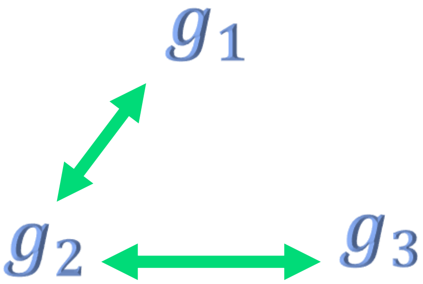
g_3	ρ_{31}	ρ_{32}	1



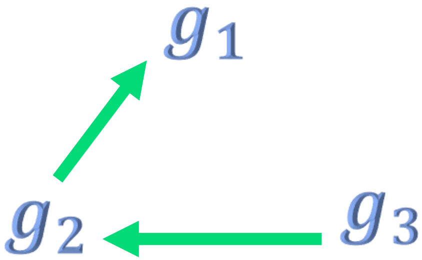
Sparse

	g_1	g_2	g_3
g_1	1	ρ_{12}	$-$
g_2	ρ_{21}	1	ρ_{23}
g_3	$-$	ρ_{32}	1



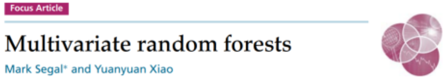
Directed

	g_1	g_2	g_3
g_1	1	$-$	$-$
g_2	ρ_{21}	1	$-$
g_3	$-$	ρ_{32}	1



Modern multi-response machinery

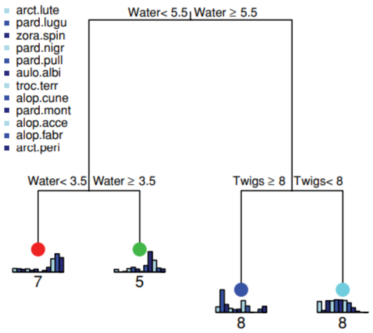
MVRF feature splits occur
for all responses together



Focus Article

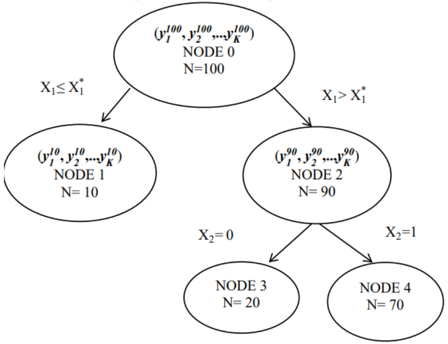
Multivariate random forests

Mark Segal* and Yuanyuan Xiao



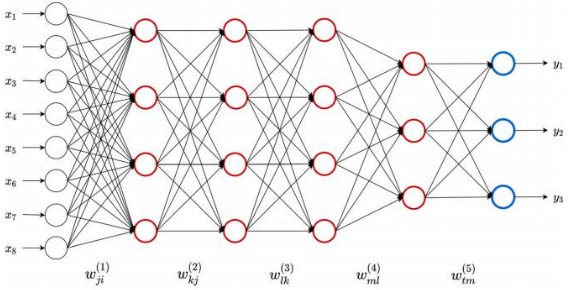
Sikdaret al. 2019. Price Dynamics on Amazon Marketplace: A Multivariate Random Forest Variable Selection approach
http://dx.doi.org/10.2139/ssrn.3518690

Figure 2. Multivariate Regression Tree

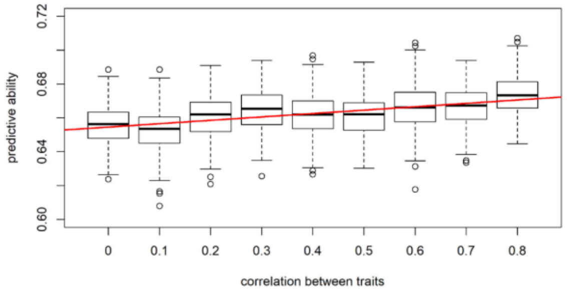


$(y_1^{100}, y_2^{100}, ..., y_K^{100})$
NODE 0
N=100
$X_1 \leq X_1^*$
$X_1 > X_1^*$
$(y_1^{10}, y_2^{10}, ..., y_K^{10})$
NODE 1
N= 10
$(y_1^{90}, y_2^{90}, ..., y_K^{90})$
NODE 2
N= 90
$X_2 = 0$
$X_2 = 1$
NODE 3
N= 20
NODE 4
N= 70

Multi-response comes natural for DNNs



Montesinos-López *et al. BMC Genomics* (2021) 22:19
https://doi.org/10.1186/s12864-020-07319-x



Using Local Convolutional Neural Networks for Genomic Prediction

Torsten Pook[1], Jan Freudenthal[2], Arthur Korte[2] and Henner Simianer[1]*

Modern multi-response machinery

MegaLMM: Mega-scale linear mixed models for genomic predictions with thousands of traits

Daniel E Runcie[1], Jiayi Qu[2], Hao Cheng[3] and Lorin Crawford[4]

MegaLMM (SEM-like approach)

$$Y = F\Lambda + XB + U + E$$

$$F = X_F B_F + U_F + E_F$$

$$Y \sim N(0, \Psi_G + \Psi_R + \Lambda'\Lambda)$$

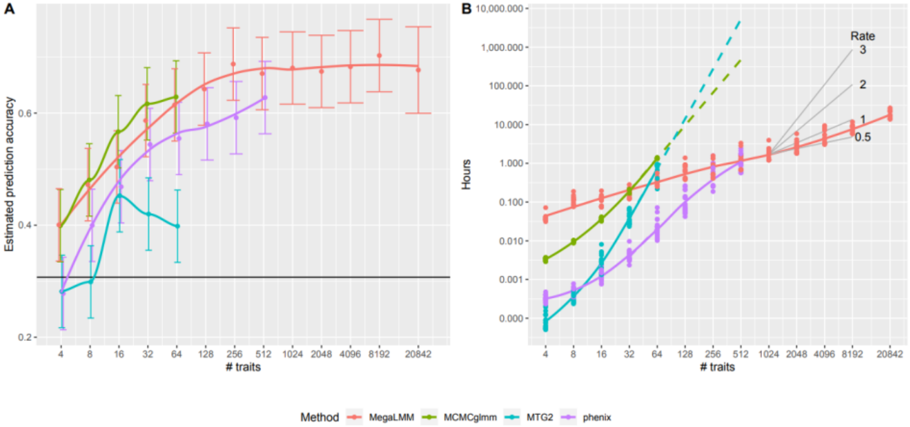
$$U \sim N(0, K, G)$$

$$G = \Psi_G + \Lambda'\Psi_{FG}\Lambda$$

$$E \sim N(0, I, R)$$

$$R = \Psi_R + \Lambda'\Psi_{FE}\Lambda$$

*Solved using Gibbs sampling



“Classical” mixed model framework has been evolving in this area

FAST COMPUTATION OF POLYGENIC EFFECTS VIA MULTIVARIATE RIDGE REGRESSION

A PREPRINT

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Tilde-Hat and Gauss-Seidel (THAGS)

Statistical model

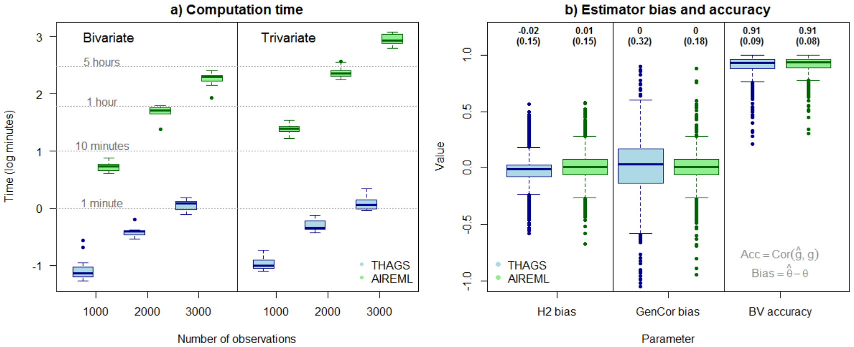
- $\mathbf{y}_k = \mu_k + \mathbf{X}_k \boldsymbol{\beta}_k + \mathbf{e}_k$, for trait k
- $\boldsymbol{\beta} \sim N(0, \mathbf{I} \otimes \boldsymbol{\Sigma}_\beta)$
- $\mathbf{e} \sim N(0, \mathbf{I} \otimes \boldsymbol{\Sigma}_e)$, $\text{cov}(\mathbf{e}_i, \mathbf{e}_j) = 0$

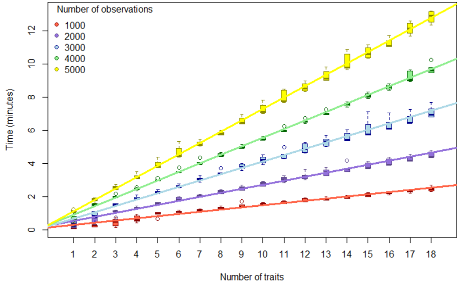
Coefficient updates: Multivariate Gauss-Seidel

- $\boldsymbol{\beta}_j^{t+1} = \left(\mathbf{X}_j'\boldsymbol{\Sigma}_e^{-1}\mathbf{X}_j + \boldsymbol{\Sigma}_\beta^{-1}\right)^{-1}\boldsymbol{\Sigma}_e^{-1}\mathbf{X}_j'(\mathbf{X}_j\boldsymbol{\beta}_j^t + \mathbf{e}^t)$
- $\mathbf{e}^{t+1} = \mathbf{e}^t - \mathbf{X}_j'(\boldsymbol{\beta}_j^{t+1} - \boldsymbol{\beta}_j^t)$

Covariance updates: Tilde-Hat method

- $\boldsymbol{\Sigma}_{\beta(A,B)} = \frac{(y_A - \hat{\mu}_A)'(X_A \hat{\beta}_B) + (y_B - \hat{\mu}_B)'(X_B \hat{\beta}_A)}{n_A \sum_{j=1}^{J} \sigma^2_{x(A)_j} + n_B \sum_{j=1}^{J} \sigma^2_{x(B)_j}}$
- $\boldsymbol{\Sigma}_{e(i,i)} = \frac{(y_i - \hat{\mu}_i)'\hat{\mathbf{e}}_i}{n_i - 1}$



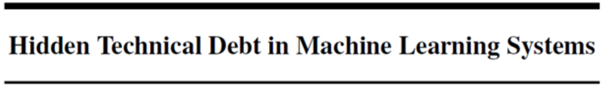


1. Good
    - Intro and motivation
    - Filters in PB
2. **Bad**
    - Metrics of success
    - Adequate validation
3. Ugly
    - Optimization
    - From RR to NN

(avoiding)

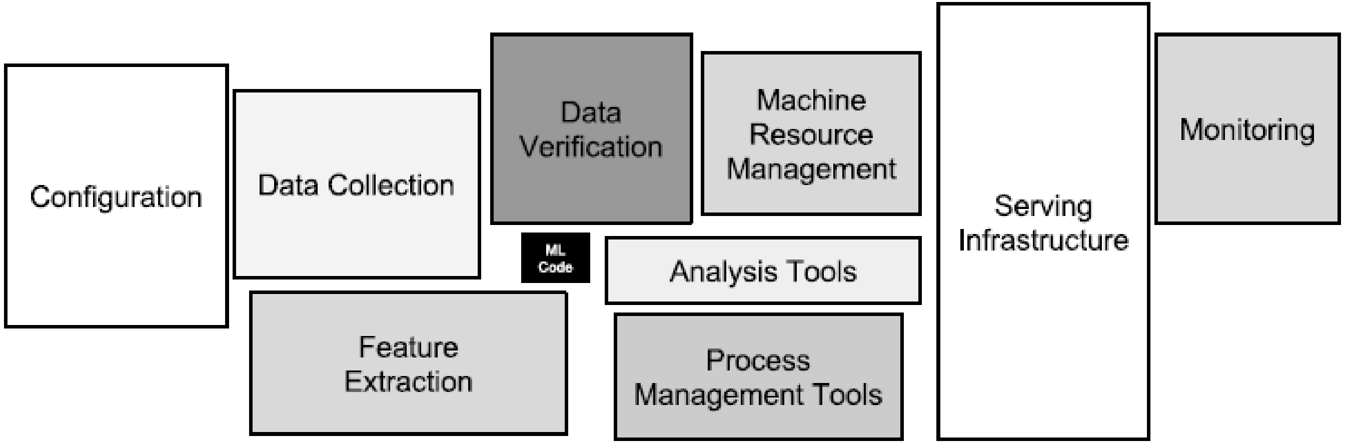
Part 2 – Bad learning

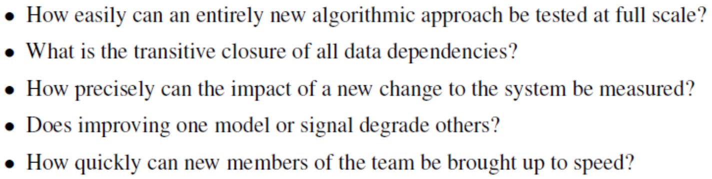
There is usually more to ML than a proof of concept with cross-validations



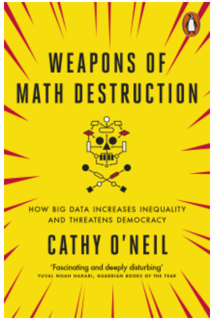
Hidden Technical Debt in Machine Learning Systems

doi/10.5555/2969442.2969519





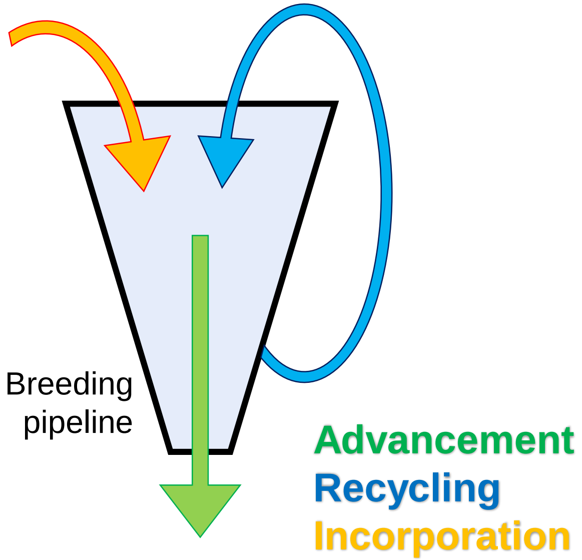
- How easily can an entirely new algorithmic approach be tested at full scale?
- What is the transitive closure of all data dependencies?
- How precisely can the impact of a new change to the system be measured?
- Does improving one model or signal degrade others?
- How quickly can new members of the team be brought up to speed?


WEAPONS OF MATH DESTRUCTION
HOW BIG DATA INCREASES INEQUALITY AND THREATENS DEMOCRACY
CATHY O'NEIL
'Fascinating and deeply disturbing'
YUVAL NOAH HARARI, GUARDIAN BOOKS OF THE YEAR

Chasing the right signal

- Breeding value (**GEBV**)
  - *Pattern*: ADDITIVE GENETICS
  - *Method*: GBLUP, BayesABC, LASSO
  - *Suits*: **RECYCLING**, **ADVANCEMENT**

- Genomic value (**EGV**)
  - *Pattern*: ANY GENETICS
  - *Method*: RKHS, DNN, Random Forest
  - *Suits*: **ADVANCEMENT**



Defining the problem: Metrics for success

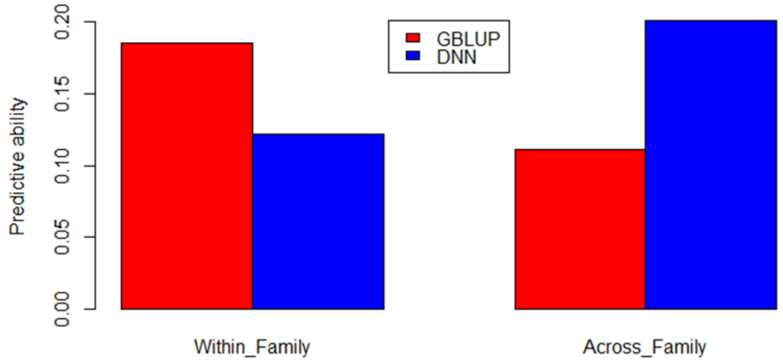
1. Scientist (**why**): to define the problem mathematically (easy to get it wrong)

2. Metric (**what**): Correlations, MSPE, Jaccard index, Accuracy, Success (1|0)

3. Testing (**how**): Simulation or cross-validation (CV) on real data? WF vs AF?

How to design an adequate cross-validation???

Two metrics, two different answers



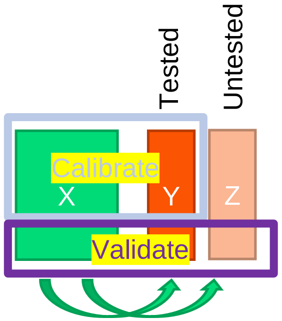
Grain yield on the SoyNAM population: Populations 1:8 predicting populations 9:15

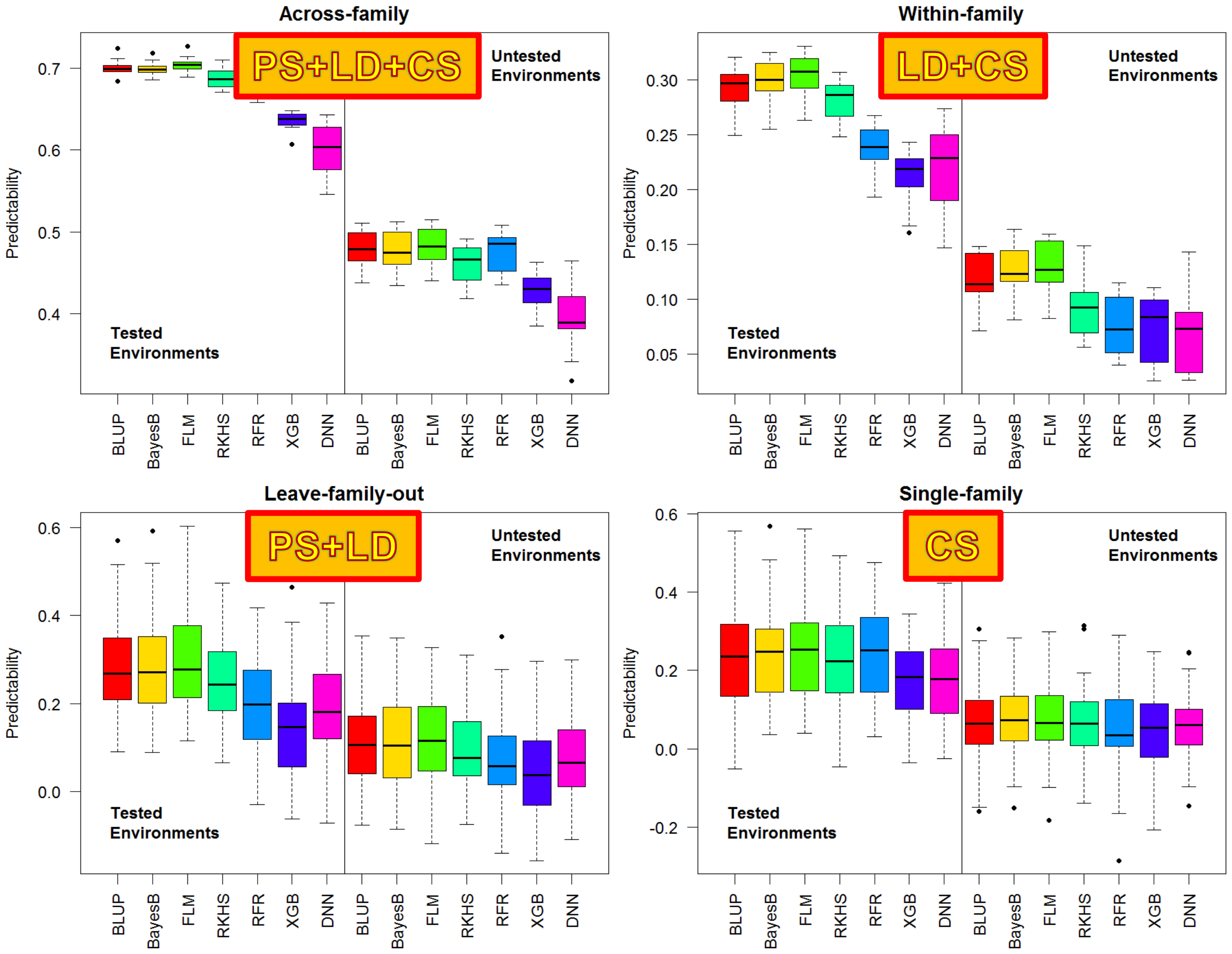
Testing machines for different scenarios of genomic prediction

	Genotype	Environment	Prediction Difficulty
CV00	New	New	*****
CV0	Observed	New	***
CV1	New	Observed	***
CV2	Observed	Observed	*

Adapted from Crossa et al. (2017) doi.org/10.1016/j.tplants.2017.08.011

CV scheme




Across-family

PS+LD+CS

Within-family

LD+CS

Leave-family-out

PS+LD

Single-family

CS

Type of information captured by SNP

- Population structure (PS)
- Linkage disequilibrium (LD)
- Cosegregation / Haplotype (CS)

SoyNAM data
ES: 2012 (7 loc)
PS: 2013 (4 loc)
#Fam = 40
Genos = 5600
SNPs = 4300
Obs: 3k-5k obs/loc

1. **Good**
    - Intro and motivation
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    - Optimization
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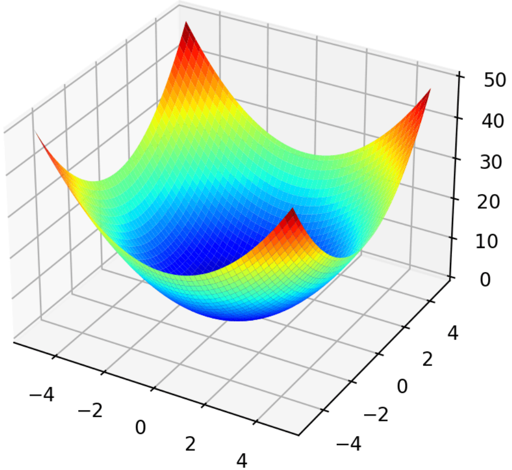
Part 3 – Ugly learning

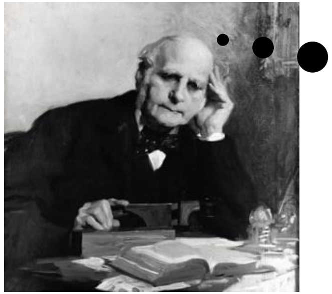
Divergency in philosophy

- In quantitative genetics:
  - Parameters: Variances + Regression coefficients
  - Function: Likelihood (complex and convex)
  - Tuning: Generally not needed
  - **Method**: First order (EM, MCMC), second order (AI, MIVQUE)
- In machine learning:
  - Parameters: Regression coefficients
  - Function: MSE, L2 (simple)
  - Tuning: Cross validations, need secondary objective function
  - **Method:** First order: coordinate & gradient descent



Solving: $\boldsymbol{y = Xb + e}$

$$Finding \rightarrow argmin(e'e + \lambda b'b)$$



I've created
a monster!!

- Coordinate descent

(Use diagonals of LHS)

$$b_j^{t+1} = \frac{x_j'(y - X_{-j}b_{-j})}{x_j'x_j + \lambda}$$

Used for WGR (RR, BayesA)

glmnet, BGLR, bWGR, GS3

- Gradient descent

(Does not build LHS)

$$b^{t+1} = b^t - \frac{2r}{n}[X'(y - Xb^t) + \lambda b^t]$$

Used for Deep Neural Nets

TF/Keras, PyTorch, MXNet, h2o

- Second order

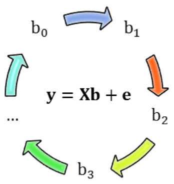
(Builds entire LHS)

$$b = (X'X + \lambda)^{-1}(X'y)$$

Used for <u>everything else</u>

ASREML, lme4, SAS, BLUPF90

Coordinate descent of a RRBLUP



$$f(b_{RR}) \rightarrow \text{argmin}\left(\sum_{i=1}^{n} e^2 + \lambda \sum_{j=1}^{p} b^2\right)$$

$$SS = e'e + \lambda(b'b\ )$$
$$SS = (y - xb)'(y - xb) + \lambda(b'b\ )$$
$$SS = y'y + (xb)'(xb) - 2(y'xb) + \lambda(b'b\ )$$
$$SS = y'y + b'(x'x)b - 2(y'xb) + \lambda(b'b\ )$$

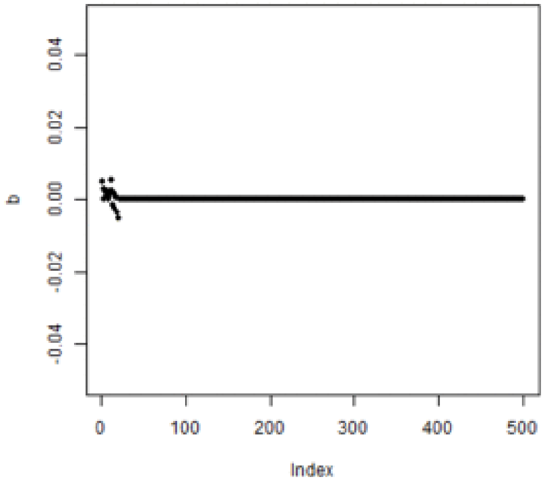
$$\frac{\partial SS}{\partial b} = \cancel{y}'\cancel{y} + 2(x'x)b^{\cancel{2}} - 2(y'x)\cancel{b} + 2\lambda b^{\cancel{2}}$$

$$0 = 2b(x'x) - 2(y'x) + 2b\lambda$$

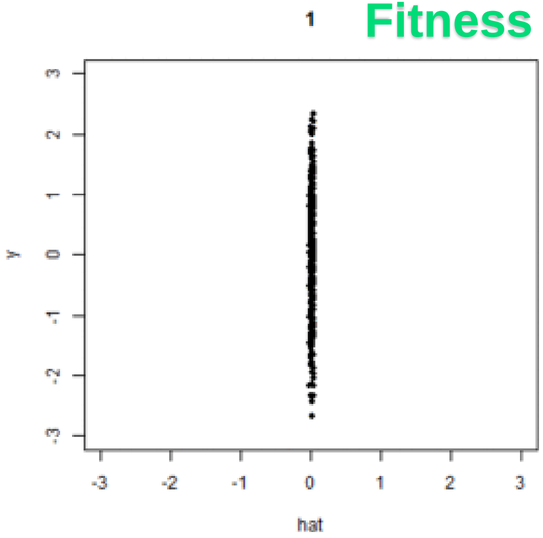
$$-2b\ (x'x + \lambda) = -2\ (y'x)$$

$$b = \frac{-2(y'x)}{-2(x'x + \lambda)} = \frac{y'x}{x'x + \lambda}$$

Marker effects



Fitness



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Corteva Biostatistics, Methods group

Gradient descent of RRBLUP

- Model (Ridge)

$$y = X\beta + e$$

- Gradient descent

$$\beta^{t+1} = \beta^{t} - \alpha\nabla$$

- Where

$$\alpha = \text{Learning rate}$$

$$f = (y - Xb)'(y - Xb) + \lambda b'b$$

$$\nabla = f' = \frac{\partial f}{\partial b} = -2X'(y - Xb) + 2\lambda b$$

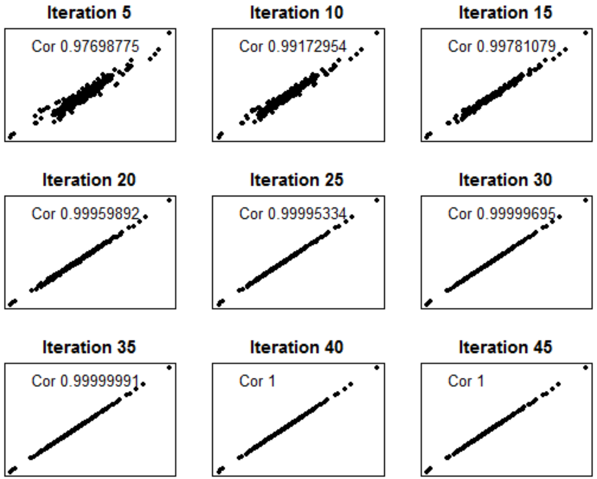
- Thus

$$\nabla = n^{-1}(-2X'e + 2\lambda\beta^{t}) = -2n^{-1}(X'e - \lambda\beta^{t})$$

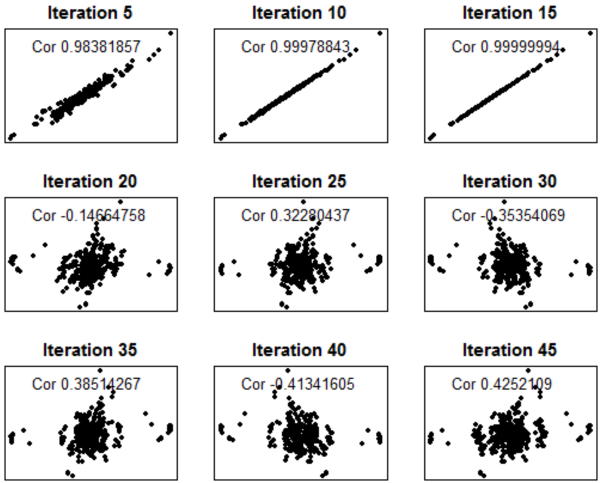
$$\boldsymbol{\beta^{t+1} = \beta^{t} + \frac{2\alpha}{n}(X'e - \lambda\beta^{t})}$$

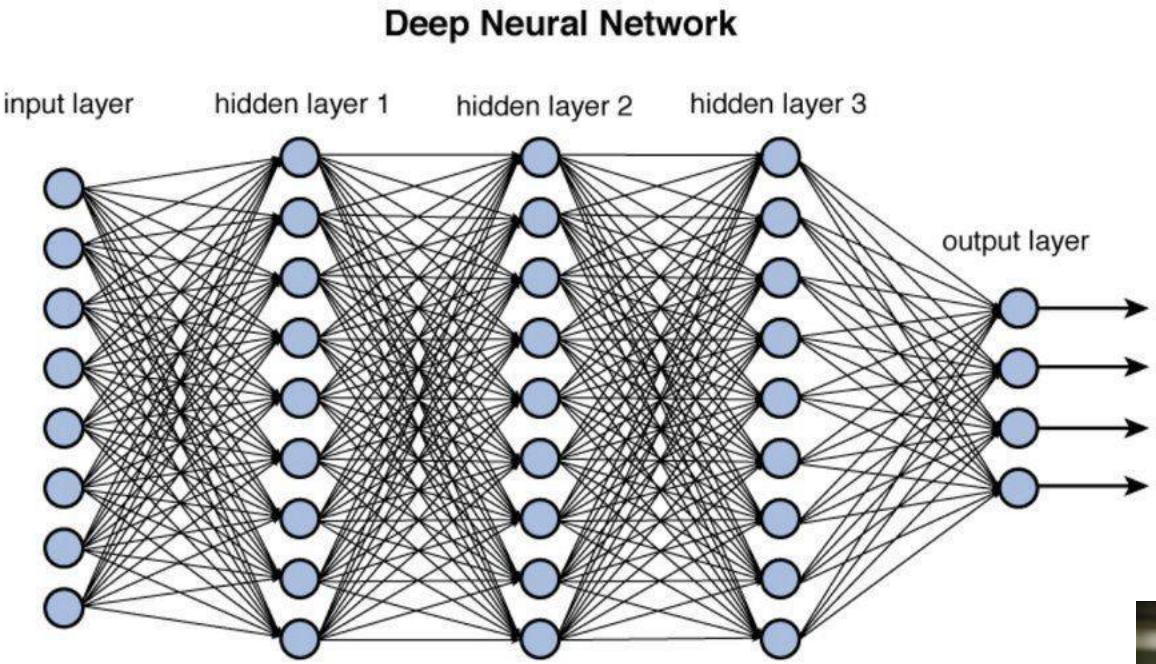
Scatter plot between true solution and solution at iteration x

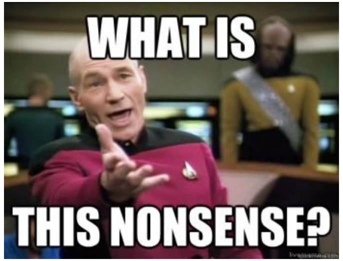
Small learning rate



Large learning rate




Deep Neural Network
input layer
hidden layer 1
hidden layer 2
hidden layer 3
output layer


WHAT IS
THIS NONSENSE?

From Ridge Regression to Deep Neural Net

Models illustrated without intercept

Linear model

$$y = Xb + e$$

PLS/PCR model

$$y = (XB_1)b_2 + e$$

NN model

$$y = \alpha(XB_1)b_2 + e$$

Deep NN model

$$y = \alpha(\alpha(XB_1)B_2)b_3 + e$$

$\alpha =$ activation function

The ~~Scary~~ Deep Neural Network

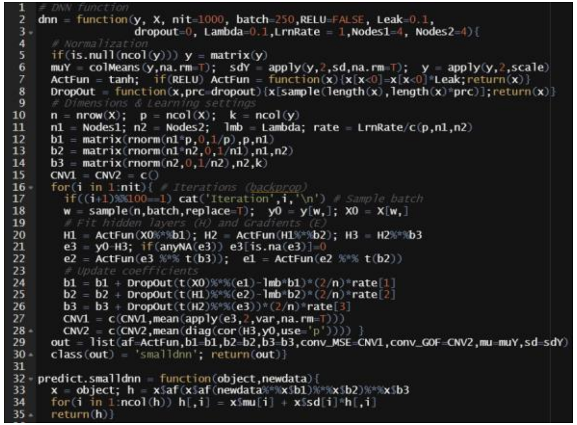
$$Y = \underbrace{\alpha(\underbrace{\alpha(\underbrace{XB_1}_{H_1})B_2}_{H_2})B_3}_{H_3} + E$$

- **Fit layers**
  - $H_1 = \alpha(XB_1)$
  - $H_2 = \alpha(H_1B_2)$
  - $H_3 = H_2B_3$

- **Compute gradients** (aka. get residuals)
  - $E_3 = Y - H3$
  - $E_2 = \alpha(E_3B_3')$
  - $E_1 = \alpha(E_2B_2')$

- **Update coefficient**
  - $B_1 = B_1 - \gamma\left(\frac{2r_1}{n}[X'E_1 - \lambda B_1]\right)$
  - $B_2 = B_2 - \gamma\left(\frac{2r_2}{n}[H_1'E_2 - \lambda B_2]\right)$
  - $B_3 = B_3 - \gamma\left(\frac{2r_3}{n}[H_2'E_3 - \lambda B_3]\right)$

Top-to-bottom code ~ 30 lines



```
# DNN function
dnn = function(y, X, nit=1000, batch=250,RELU=FALSE, Leak=0.1,
               dropout=0, Lambda=0.1,LrnRate = 1,Nodes1=4, Nodes2=4){
  # Normalization
  if(is.null(ncol(y))) y = matrix(y)
  muY = colMeans(y,na.rm=T);  sdY = apply(y,2,sd,na.rm=T);  y = apply(y,2,scale)
  ActFun = tanh;  if(RELU) ActFun = function(x){x[x<0]=x[x<0]*Leak;return(x)}
  DropOut = function(x,prc=dropout){x[sample(length(x),length(x)*prc)];return(x)}
  # Dimensions & Learning settings
  n = nrow(X);  p = ncol(X);  k = ncol(y)
  n1 = Nodes1; n2 = Nodes2;  lmb = Lambda; rate = LrnRate/c(p,n1,n2)
  b1 = matrix(rnorm(n1*p,0,1/p),p,n1)
  b2 = matrix(rnorm(n1*n2,0,1/n1),n1,n2)
  b3 = matrix(rnorm(n2,0,1/n2),n2,k)
  CNV1 = CNV2 = c()
  for(i in 1:nit){ # Iterations (backprop)
    if((i+1)%%100==1) cat('Iteration',i,'\n') # Sample batch
    w = sample(n,batch,replace=T);  y0 = y[w,]; X0 = X[w,]
    # Fit hidden layers (H) and Gradients (E)
    H1 = ActFun(X0%*%b1); H2 = ActFun(H1%*%b2); H3 = H2%*%b3
    e3 = y0-H3; if(anyNA(e3)) e3[is.na(e3)]=0
    e2 = ActFun(e3 %*% t(b3));  e1 = ActFun(e2 %*% t(b2))
    # Update coefficients
    b1 = b1 + DropOut(t(X0)%*%(e1)-lmb*b1)*(2/n)*rate[1]
    b2 = b2 + DropOut(t(H1)%*%(e2)-lmb*b2)*(2/n)*rate[2]
    b3 = b3 + DropOut(t(H2)%*%(e3))*(2/n)*rate[3]
    CNV1 = c(CNV1,mean(apply(e3,2,var,na.rm=T)))
    CNV2 = c(CNV2,mean(diag(cor(H3,y0,use='p')))) }
  out = list(af=ActFun,b1=b1,b2=b2,b3=b3,conv_MSE=CNV1,conv_GOF=CNV2,mu=muY,sd=sdY)
  class(out) = 'smalldnn'; return(out)}

predict.smalldnn = function(object,newdata){
  x = object; h = x$af(x$af(newdata%*%x$b1)%*%x$b2)%*%x$b3
  for(i in 1:ncol(h)) h[,i] = x$mu[i] + x$sd[i]*h[,i]
  return(h)}
```

Thank you for your attention!

Remarks:

1) ML can be a powerful tool for plant breeding
2) Cross-validation must be carefully design to understand the machinery
3) The scary black boxes are usually simple methods

Questions??

Alencar Xavier

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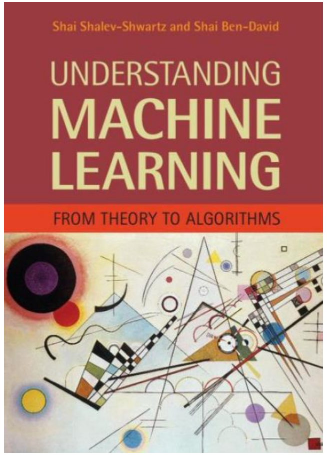
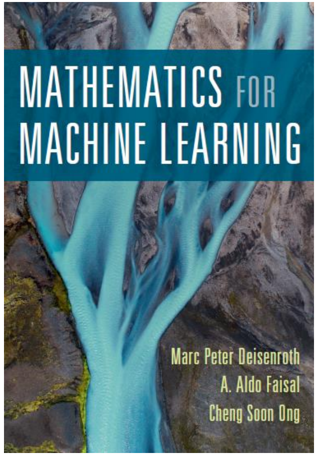
Some free lit to look up!



Shai Shalev-Shwartz and Shai Ben-David

UNDERSTANDING MACHINE LEARNING

FROM THEORY TO ALGORITHMS



MATHEMATICS FOR MACHINE LEARNING

Marc Peter Deisenroth
A. Aldo Faisal
Cheng Soon Ong

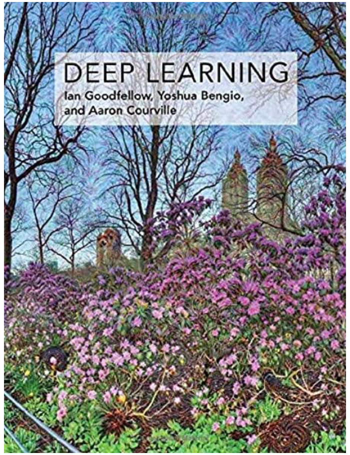
Computational and Statistical Advances in Testing and Learning

Aaditya Kumar Ramdas

July 2015
CMU-ML-15-101

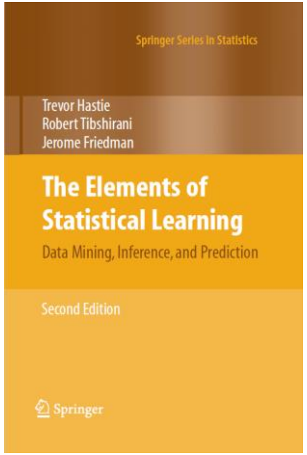
ML MACHINE LEARNING DEPARTMENT

Carnegie Mellon.



DEEP LEARNING

Ian Goodfellow, Yoshua Bengio, and Aaron Courville



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