Statistical Inference vs. Machine Learning: Why can't we be friends?

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LDI Journal Club

Motivation

This Guy

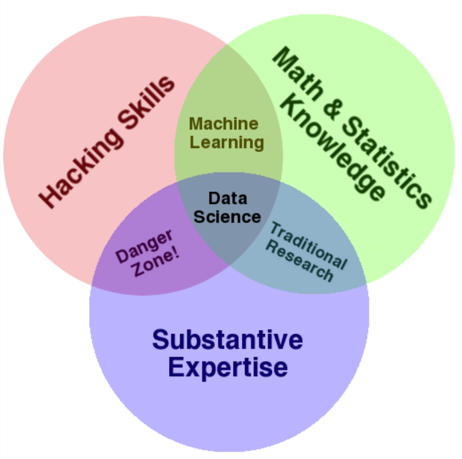
Two Cultures

Statistical Science
2001, Vol. 16, No. 3, 199–231

Statistical Modeling: The Two Cultures

Leo Breiman

Data Science Venn Diagram[1]

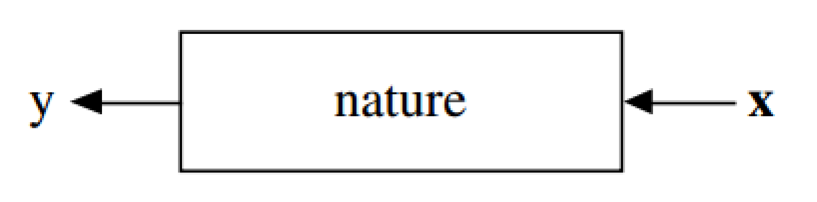


[1] http://drewconway.com/zia/2013/3/26/the-data-science-venn-diagram

Statistical Learning

Nature Functions to Associate X with y[2]

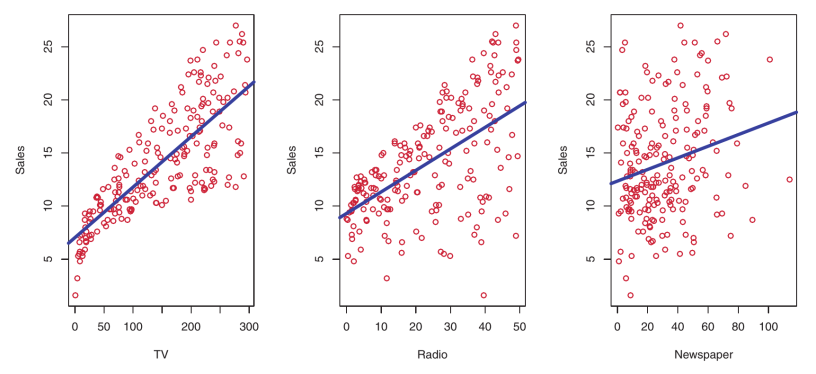
- A matrix of input variables **X** go in one side
- On the other side, response variable **y** comes out



[2] Breiman, Leo. *Statistical modeling: The two cultures*. Statistical science (2001)

Example: Advertising Data Set

- y: `sales` of a product in 200 different markets (*response or dependent variable*)
- $\mathtt{X} = (X_1, X_2, X_3)$: advertising budgets for `TV, radio, newspaper` (*predictors, independent variables, features*)



Model Set-up

- We observe a quantitative response Y and p different predictors $X = (X_1, \ldots, X_p)$
- ε is an error term independent of X with mean 0
- We assume there is some relationship between Y and X:

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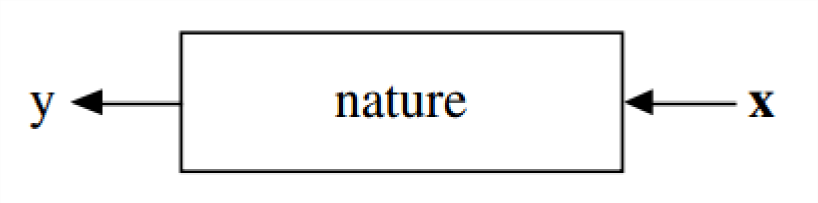
- We assume there is some relationship between Y and X:

$$Y = f(X) + \varepsilon$$

What is f?



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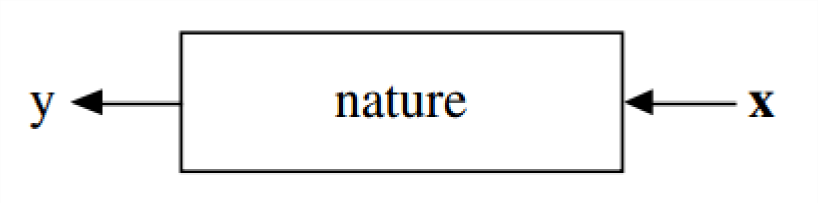

- f is *nature*

What is f

- f is a function that connects X to y and is generally unknown

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What is f

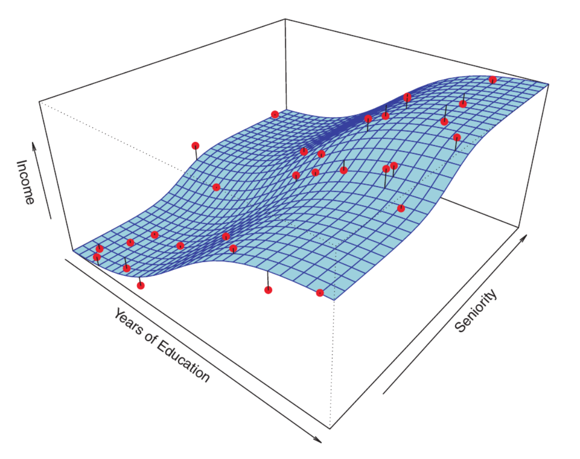
- f is a function that connects X to y and is generally unknown
- In this situation, one must estimate f based on observed points
- $\widehat{f}$ denotes our estimate to f

Exercise: Income dataset

- `income` is the response

Exercise: Income dataset

- `income` is the response
- $\widehat{f}(x) = 1.4 \times \text{Years of Education} + 0.56 \times \text{Seniority}^2$



Statistical Learning refers to a set of approaches for estimating f

Two Cultures: Prediction and Inference

Author of Random Forests:

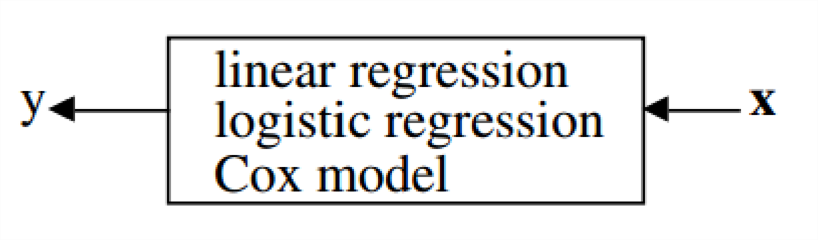
Statistical Science
2001, Vol. 16, No. 3, 199–231

Statistical Modeling: The Two Cultures

Leo Breiman

Data Modelling Culture[3]

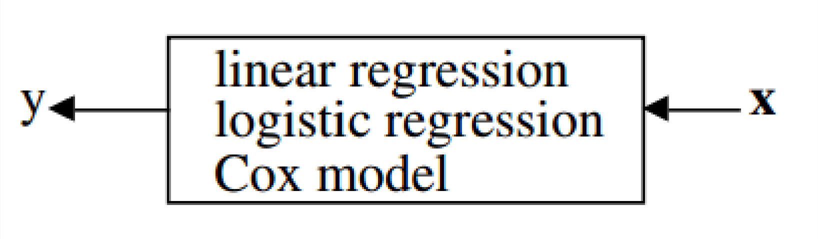
- Starts with assuming a stochastic data model for the inside of the box (e.g. normal, binomial)
- Values of the parameters are estimated from the data
- Information (ORs, HRs)



[3] Breiman, Leo. *Statistical modeling: The two cultures.* Statistical science (2001)

Data Modelling Culture Criticisms

- The belief that by imagination and by looking at the data, can invent a good parametric model for a complex mechanism devised by nature



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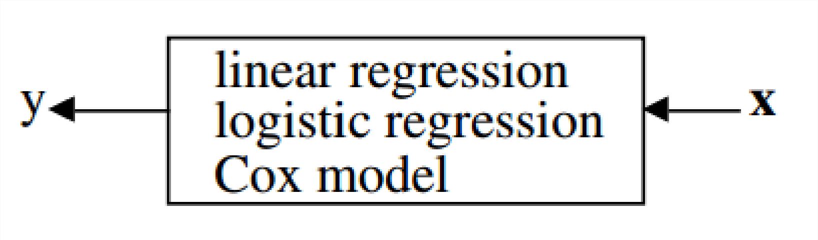

- Conclusions are about the model's mechanisms, not nature's
- If the model is a poor emulation of nature, the conclusions maybe wrong

The American Statistician

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The ASA's Statement on p-Values: Context, Process, and Purpose

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Data Modelling Culture Criticisms: Reliance on *P*-values

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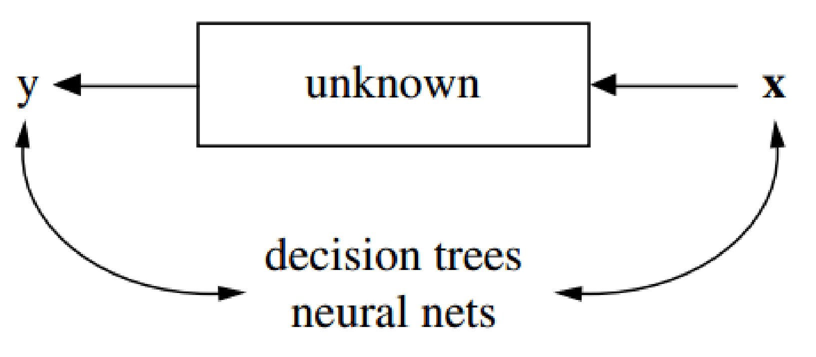
The ASA's Statement on p-Values: Context, Process, and Purpose

Ronald L. Wasserstein & Nicole A. Lazar

- *P*-values do not measure the probability that the studied hypothesis is true - *P*-values can indicate how incompatible the data are with a specified statistical model

Algorithmic Modelling Culture[4]

- Considers the inside of the box **complex** and **unknown**
- Find an algorithm that operates on X to predict y
- Prediction



[4] Breiman, Leo. *Statistical modeling: The two cultures*. Statistical science (2001)

Algorithmic Modelling Culture Criticisms[5]

[5] XKCD comic

Why Estimate f ?

Two Reasons

Prediction

- Machine Learning, Neural Nets, Support Vector Machines, Random Forests

Two Reasons

Prediction

- Machine Learning, Neural Nets, Support Vector Machines, Random Forests

Inference

- Linear, Logistic, Cox Regression

Prediction

Prediction

- In many situations, a set of inputs X are readily available, but the output Y cannot easily be obtained
- We can predict Y using

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- Example: Refer to Brent's talk on deep neural networks and putting pathologists out of work

_computational BIOLOGY

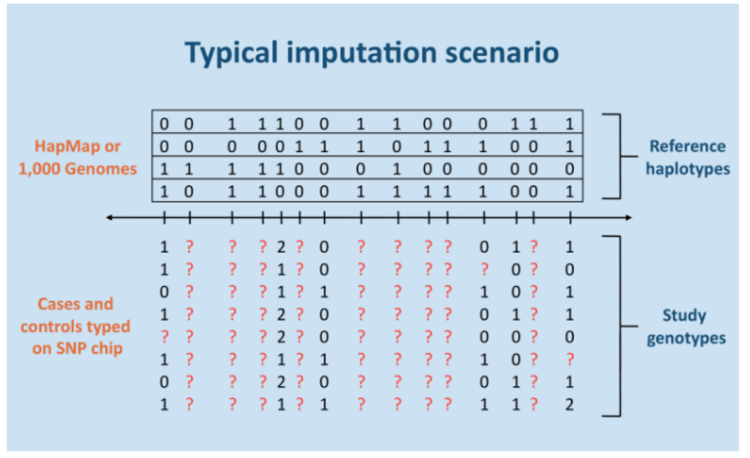
nature biotechnology

ANALYSIS

OPEN

Large-scale imputation of epigenomic datasets for systematic annotation of diverse human tissues

Jason Ernst[1–5] & Manolis Kellis[6,7]

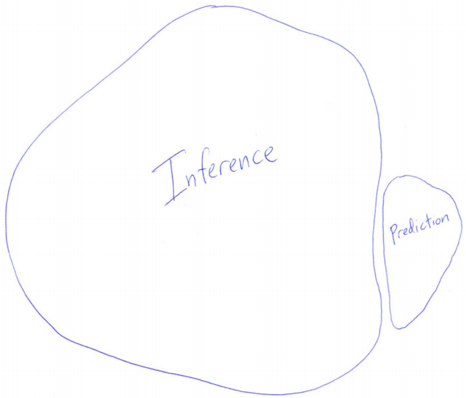

Typical imputation scenario
HapMap or
1,000 Genomes
0 0 1 1 1 0 0 1 1 0 0 0 1 1 1
0 0 0 0 0 1 1 1 0 1 1 1 0 0 1
1 1 1 1 1 0 0 0 1 0 0 0 0 0 0
1 0 1 1 0 0 0 1 1 1 1 1 0 0 1
Reference
haplotypes
Cases and
controls typed
on SNP chip
1 ? ? ? 2 ? 0 ? ? ? ? 0 1 ? 1
1 ? ? ? 1 ? 0 ? ? ? ? ? 0 ? 0
0 ? ? ? 1 ? 1 ? ? ? ? 1 0 ? 1
1 ? ? ? 2 ? 0 ? ? ? ? 0 1 ? 1
? ? ? ? 2 ? 0 ? ? ? ? 0 0 ? 0
1 ? ? ? 1 ? 1 ? ? ? ? 1 0 ? ?
0 ? ? ? 2 ? 0 ? ? ? ? 0 1 ? 1
1 ? ? ? 1 ? 1 ? ? ? ? 1 1 ? 2
Study
genotypes

Inference

Inference

- We are often interested in understanding the way that Y is affected as $X_1, \ldots, X_p$ change
- Which predictors are associated with the response
- $\widehat{f}$ can no longer be treated as a black box
- Examples: GWAS, EWAS

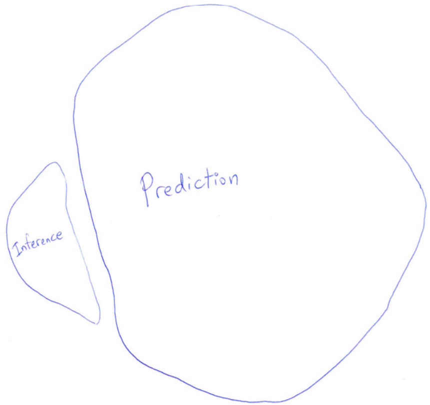
Statistics vs. Machine Learning[6]



How statisticians see the world?

[6] source: http://statweb.stanford.edu/ tibs/ftp/nips2015.pdf

Statistics vs. Machine Learning[7]



How machine learners see the world?

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Case Study

UK Biobank

biobank uk

Improving the health of future generations

The Data

- GWAS for Z-Score BMD conducted by John Morris et. al (*Nature Genetics 2017*)
- Covariates: Age, Sex, PC1, PC2, PC3, PC4
- GWAS Hits: 301 Conditionally Independent SNPs
- Control SNPs: 10k SNPs (LD < 0.10 with lead SNPs)
- Dosages were calculated from `BGEN` files using `qctool`
- Training Data: $\sim$ 115k Observations (80%)
- Test Data: $\sim$ 30k Observations (20%)

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```
pryr::mem_used()
7.08 GB
```

Finding SNPs in low LD with lead SNPs

- Not looking for tag SNPs.
- Used a plink function to find all genotyped SNPs with LD > 0.1 with at least one of the 301 lead SNPs.
- `–r2 inter-chr –ld-window-r2 0.1 –ld-snp-list leadSNPs`
- Randomly selected 10K SNPs from all available excluding the ones found in the previous step.

The Data

	ID_1	zbmd	PC1	PC2	PC3	PC4	age	sex	rs139603701	rs2708632	rs75077113
1	2610781	-1.255	-7.42628	-3.3967600	-4.6292400	3.19530000	63	0	0.00000000	1.0000000	0.00000000
2	4114347	-0.339	-6.45636	-0.5157170	-0.3762300	-1.28798000	65	0	0.00000000	1.0000000	0.07400510
3	4399930	-0.600	-6.74236	-1.2213700	-2.5755200	4.34368000	66	1	0.00000000	1.0000000	0.00000000
4	2081319	0.809	-6.05389	-0.4911940	-2.0864600	5.37939000	48	0	0.00000000	1.0000000	0.00000000
5	1347380	0.279	-5.52867	-1.2864200	-3.2811600	0.45690000	53	0	0.00000000	2.0000000	1.00000000
6	3262449	-0.421	-6.67005	-0.9253650	-0.4240550	10.36690000	66	1	0.00000000	2.0000000	0.00100708
7	4870063	-0.454	-8.41719	-1.4366200	-1.6072600	-1.29085000	43	1	0.00000000	2.0000000	0.99700900
8	1141212	1.383	-8.73178	-1.6209500	-2.6827300	-2.02636000	65	1	0.00000000	2.0000000	0.02301030
9	2997954	-2.290	-5.55814	-0.4710770	-1.3477500	-0.09621100	68	1	0.00000000	1.0000000	0.00100708
10	5805218	2.289	-9.22547	-3.7621800	-1.2818900	2.37689000	63	1	0.04199220	1.0000000	0.02499390

Methods

Domain	Method	Interpretable	Feature
Stat	`lm`	✓	No selection, p-values
	`ridge`	✓	No selection, shrinks coefficients
	`lasso`	✓	Variable selection and shrinkage
	`enet`	✓	Variable selection and shrinkage
ML	`Random Forest`	✓	Variable importance
	`Neural Net`	✗	Lots of choices to make

Models

1. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4`

Models

1. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4`
2. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP`

Models

1. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4`
2. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP`
3. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 300 Control`

Models

1. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4`
2. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP`
3. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 300 Control`
4. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 1k Control`

Models

1. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4`
2. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP`
3. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 300 Control`
4. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 1k Control`
5. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 5k Control`

Models

1. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4`
2. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP`
3. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 300 Control`
4. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 1k Control`
5. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 5k Control`
6. `zbmd ~ age + sex + PC1 + PC2 + PC3 + PC4 + 301 lead SNP + 10k Control`

```r
lm(lcavol ~ ., data=Prostate)
```

```
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     -2.260      1.260    -1.8     0.08 .
## lweight         -0.073      0.174    -0.4     0.68
## age              0.023      0.011     2.1     0.04 *
## lbph            -0.087      0.058    -1.5     0.14
## svi             -0.154      0.254    -0.6     0.55
## lcp              0.367      0.082     4.5    2e-05 ***
## gleason          0.191      0.154     1.2     0.22
## pgg45           -0.007      0.004    -1.7     0.10
## lpsa             0.573      0.086     6.7    2e-09 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0
```

Penalized Model (Lasso, Elastic Net, Ridge)

```r
cv.glmnet(X, Y)
```

```
## 9 x 1 sparse Matrix of class "dgCMatrix"
##                     1
## (Intercept) 0.3708615
## lweight     .
## age         .
## lbph        .
## svi         .
## lcp         0.2293733
## gleason     .
## pgg45       .
## lpsa        0.4116749
```

Machine Learning Model: Random Forest

- Used the R package `ranger`, which allows parallel computing.
- Build 1000 trees (using 5,000 crashed with 10,000 control SNPs)
- Used the distribution of variable importance measures to perform variable selection.
- No need to normalize.

```
> pred_rf_mod3
Ranger prediction

Type:                             Regression
Sample size:                      29139
Number of independent variables:  607
> rf_mod3
Ranger result

Call:
 ranger(formula = mod3_fmla, data = ukb_train, importance = "impurity")

Type:                             Regression
Number of trees:                  500
Sample size:                      116571
Number of independent variables:  607
Mtry:                             24
Target node size:                 5
Variable importance mode:         impurity
OOB prediction error (MSE):       0.9209093
R squared (OOB):                  0.08068676
```

Figure 1: Output

Random Forest: Variable Importance

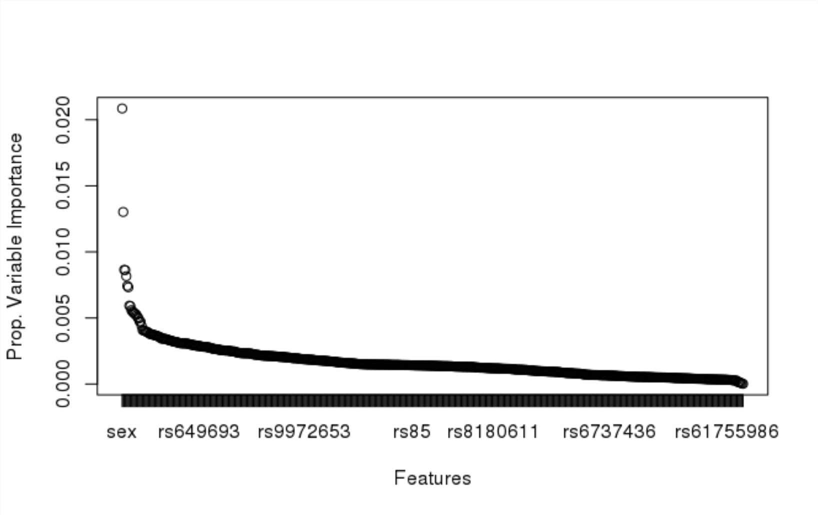


Figure 2: Variable importance

MLM: Support vector machine

- Tried two R packages without success (e1071 with function svm, and parallelSVM).
- It seems that we have too many observations (svm might be more suited when $N << p$)

MLM: Deep Neural Network

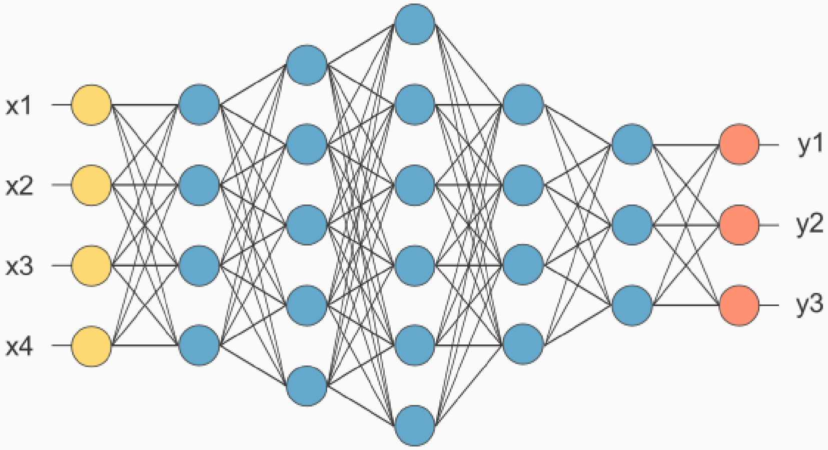
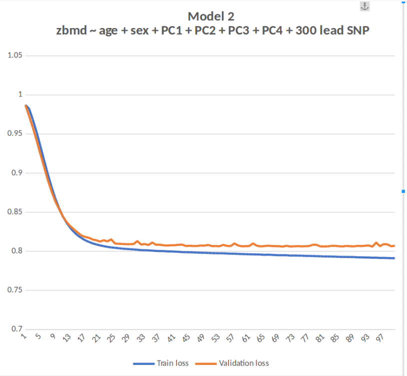
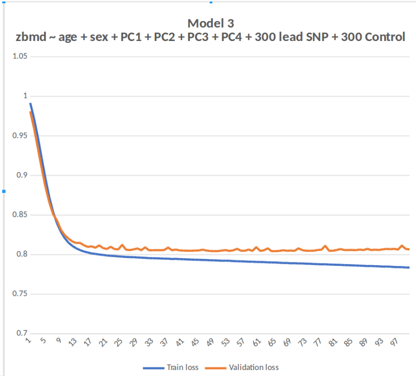


Figure 3: Deep Neural Network

Deep Neural Network (keras + Theano)





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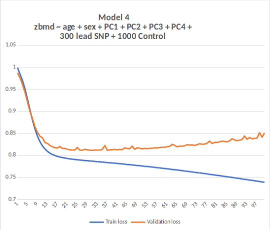
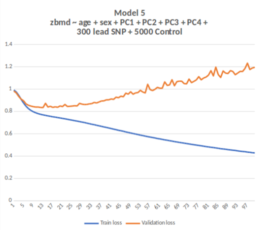
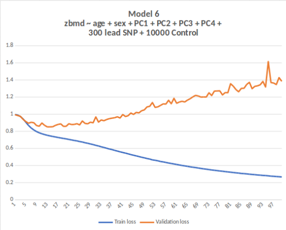






Results: R2

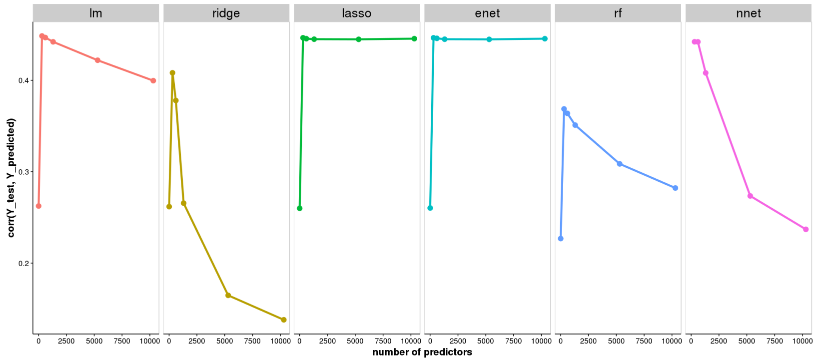


Figure 4: R2 vs. No. of Predictors

Results: Sensitivity vs. Specificity

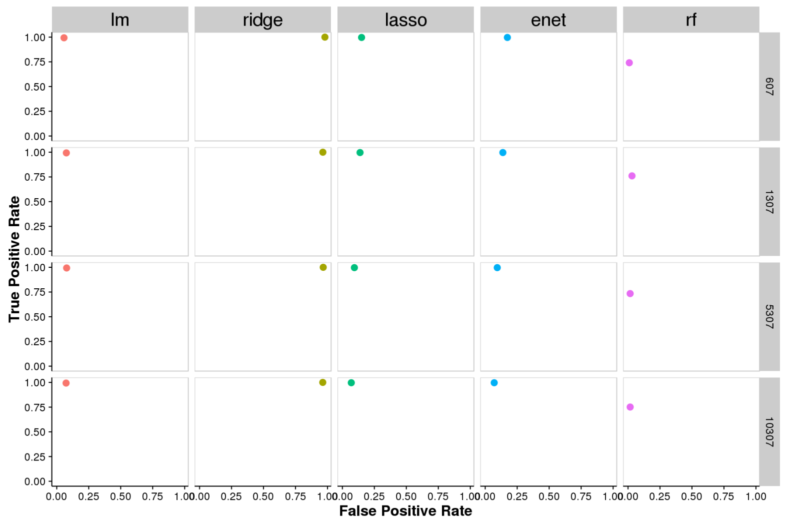


Figure 5: True Positive Rate vs. False Positive Rate

Results: Timings

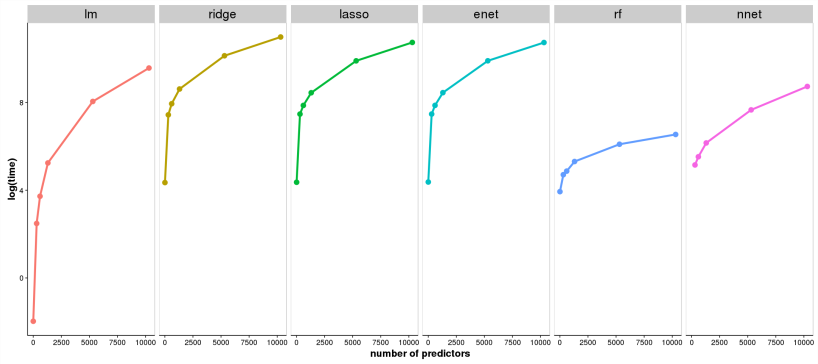


Figure 6: Time vs. No. of Predictors

Three Lessons to be Learned: Rashomon, Occam and Bellman

Rashomon

- Japanese movie (1950) in which four people, from different vantage points, witness a murder and a rape.
- When testifying, they all report the same facts, but their stories of what happened are very different

Rashomon: Many models give same $\hat{y}$, but tell different story

Model 1

$$y = 2.1 + 3.8x_3 - 0.6x_8 + 83.2x_{12}$$

Model 2

$$y = -8.9 + 4.6x_5 + 0.01x_6 + 12x_{15}$$

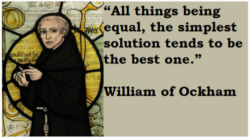
Model 3

$$y = -76.7 + 9.3x_2 + 22x_7 - 13.2x_8$$

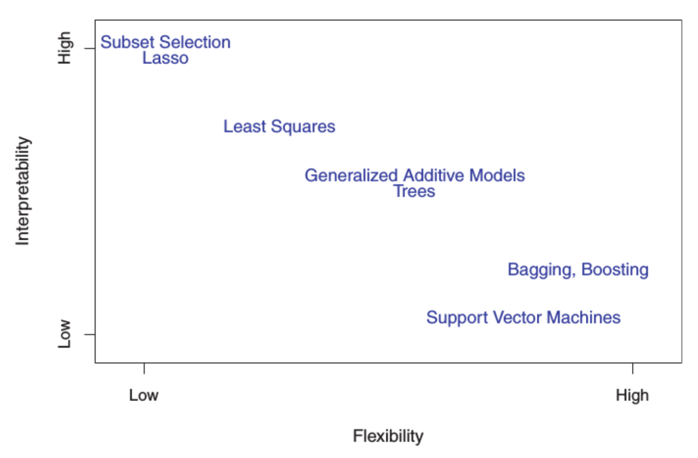
- All produce test set error within 1% of each other
- Which one is better?

Occam

- Unfortunately, in prediction, accuracy and simplicity (interpretability) are in conflict



Trade-off b/w Prediction Accuracy & Model Interpretability[8]



[8] Introduction to Statistical Learning

Bellman: Curse of Dimensionality

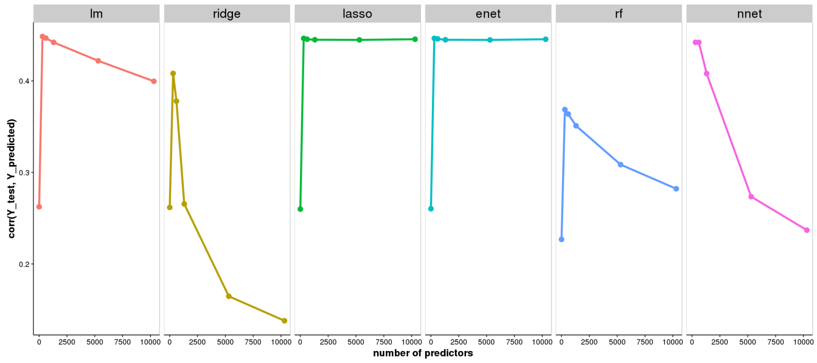


Figure 7: R2 vs. No. of Predictors

Final Thoughts

Take Home Message #1

- Ignore these terms: Machine Learning, Big Data, Statistical Learning

- Ignore these terms: **Machine Learning, Big Data, Statistical Learning**
- Focus on the input and output of a method

Take Home Message #1

- Ignore these terms: Machine Learning, Big Data, Statistical Learning
- Focus on the input and output of a method
- Ignore the arbitrary classification it falls under

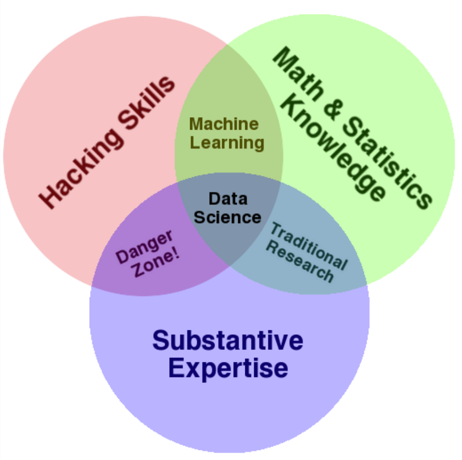
Take Home Message #2

- Focus on the goal of the study
- Inference
- Prediction
- or Both

- Inference and Prediction are both very challenging

Take Home Message #3

- Stay away from the Danger Zone



References

ISL

www-bcf.usc.edu/~gareth/ISL/

An Introduction to Statistical Learning

with Applications in R

Gareth James, Daniela Witten, Trevor Hastie and Robert Tibshirani

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ISLR Package

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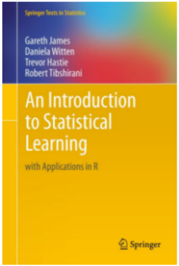
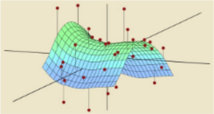
Author Bios

Errata



Download the book PDF
(corrected 6th printing)



Statistical Learning MOOC covering the entire ISL book offered by Trevor Hastie and Rob Tibshirani. Start anytime in self-paced mode.

Leo Breiman (1928 - 2005)

Appendix

How accurate is $\widehat{Y}$

- The accuracy of $\widehat{Y}$ depends on two quantities

$$mean(Y - \widehat{Y})^2 = \underbrace{[f(X) - \widehat{f}(X)]^2}_{reducible} + \underbrace{Variance(\varepsilon)}_{Irreducible}$$

How accurate is $\widehat{Y}$

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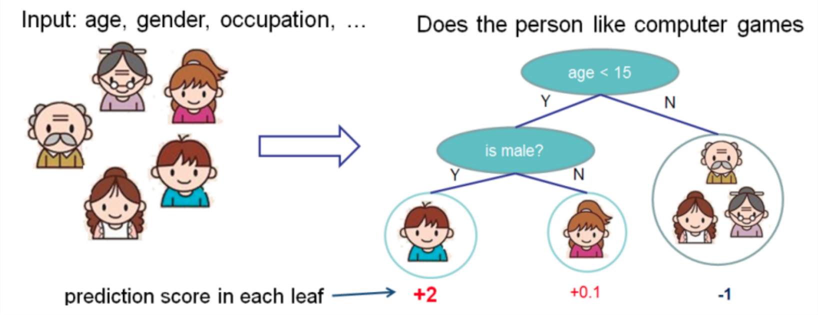
$$mean(Y - \widehat{Y})^2 = \underbrace{[f(X) - \widehat{f}(X)]^2}_{reducible} + \underbrace{Variance(\varepsilon)}_{Irreducible}$$

- Goal of most learning techniques is to estimate f with the aim of minimizing the reducible error

Trees

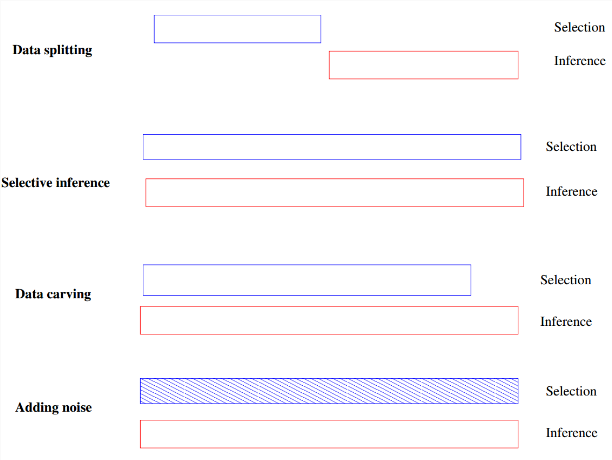

Input: age, gender, occupation, ...
Does the person like computer games
age < 15
Y
N
is male?
Y
N
prediction score in each leaf
+2
+0.1
-1

How do we Estimate f?

- Linear model

$$f(X) = \beta_0 + \beta_1 X_1 + \beta_2 X_2$$

Inference Techniques[9]



[9] source: http://statweb.stanford.edu/ tibs/ftp/nips2015.pdf