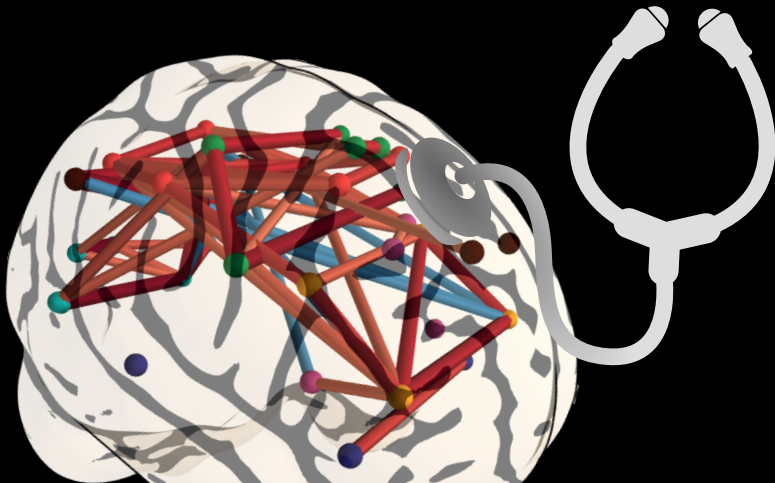


Advanced machine learning for neuroimaging

Gaël Varoquaux

McGill

Inria



- 1 Large scale**
- 2 Some advanced estimators**
- 3 Advanced learners on brain images**
- 4 Machine learning principles**

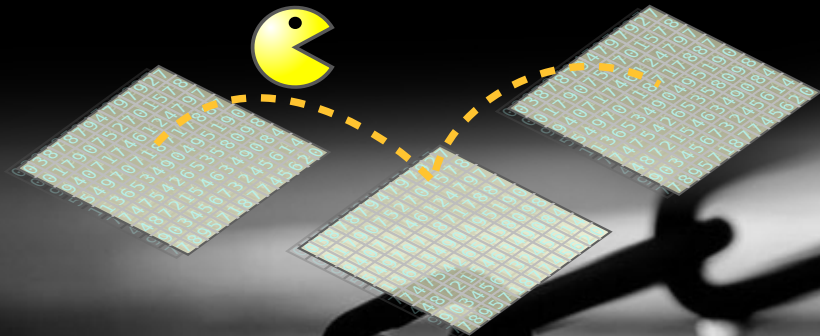
1 Large scale

Difficulty: the data do not fit in memory

See also: <http://www.slideshare.net/GaelVaroquaux/processing-bigish-data-on-commodity-hardware-simple-python-patterns>

1 On-line algorithms

```
estimator.partial_fit(X_train, Y_train)
```



1 On-line algorithms

```
estimator.partial_fit(X_train, Y_train)
```

Linear models

```
sklearn.linear_model.SGDRegressor  
sklearn.linear_model.SGDClassifier
```

SGD = Stochastic gradient descent



Different losses, different penalties

learning rate 😞

1 On-line algorithms

```
estimator.partial_fit(X_train, Y_train)
```

Linear models

```
sklearn.linear_model.SGDRegressor  
sklearn.linear_model.SGDClassifier
```

Clustering

```
sklearn.cluster.MiniBatchKMeans  
sklearn.cluster.Birch      (new in 0.16)
```

PCA (new in 0.16)

```
sklearn.decompositions.IncrementalPCA
```

1 On-the-fly data reduction

Many features

⇒ Reduce the data as it is loaded

```
X_small = estimator.transform(X_big, y)
```



1 On-the-fly data reduction

Random projections (will average features)

`sklearn.random_projection`

random linear combinations of the features

Fast clustering of features

`sklearn.cluster.FeatureAgglomeration`

on images: super-pixel strategy

Hashing when observations have varying size (e.g. words)

`sklearn.feature_extraction.text.`

`HashingVectorizer`

1 On-the-fly data reduction

Hashing when observations have varying size
(e.g. words)

```
sklearn.feature_extraction.text.  
HashingVectorizer
```

TF-IDF needs

- to know the vocabulary
- to count everybody

⇒ multiple passes on the data

Hashing avoids that

but no IDF normalization

Use an LDA, and not an NMF

+ stateless: can be used in parallel

2 Some advanced estimators



[Neurosynth, Neuroquery]

Linear estimators

- Can handle large number of features
- Typically a logistic regression

`sklearn.linear_model.LogisticRegression`
`sklearn.linear_model.LogisticRegressionCV`
'l2' and 'l1' penalties different solvers

`sklearn.linear_model.SGDClassifier`
For on-line estimator

Naive Bayes

- Very good for many classes
- On-line estimator

+ **chi2 feature selection**

2 For heterogeneous columnar data

Priceless for tabular data eg socio-demographics

- Tree methods are good:

robust to strange data distributions

- Ensemble methods: need to combine many trees

Random forests

`sklearn.ensemble.RandomForestClassifier`

`sklearn.ensemble.ExtraTreesClassifier`

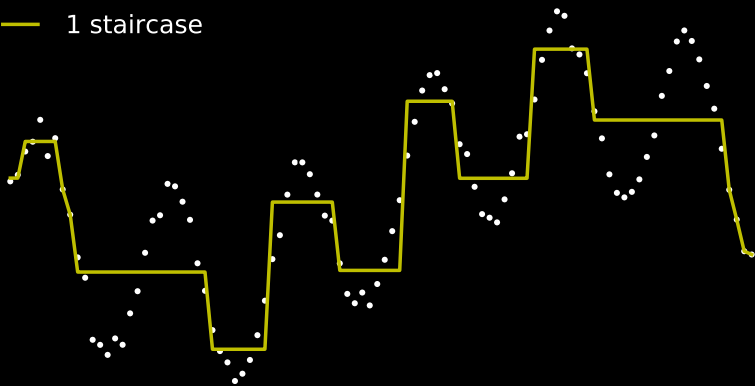
Boosted trees

`sklearn.ensemble.HistGradientBoostingClassifier`

Native support for missing values

2 Gradient-boosted regression trees

— 1 staircase

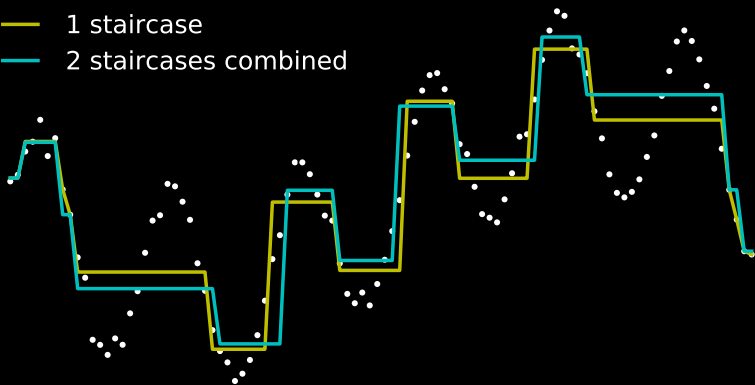


■ Fit with a tree of depth 10

staircase of 10 constant values

2 Gradient-boosted regression trees

- 1 staircase
- 2 staircases combined



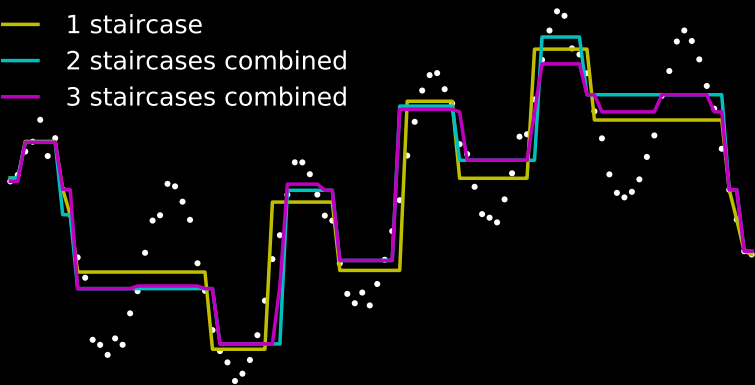
- Fit with a tree of depth 10

staircase of 10 constant values

- Fit a new tree on errors

2 Gradient-boosted regression trees

- 1 staircase
- 2 staircases combined
- 3 staircases combined

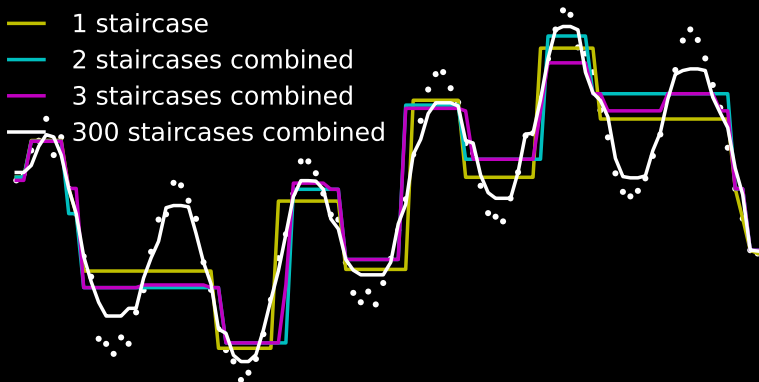


- Fit with a tree of depth 10

staircase of 10 constant values

- Fit a new tree on errors
- Keep going

2 Gradient-boosted regression trees



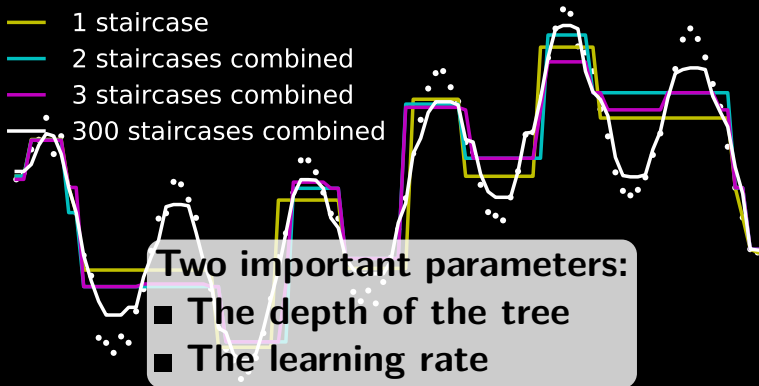
- Fit with a tree of depth 10

staircase of 10 constant values

- Fit a new tree on errors
- Keep going

Boosted regression trees

2 Gradient-boosted regression trees



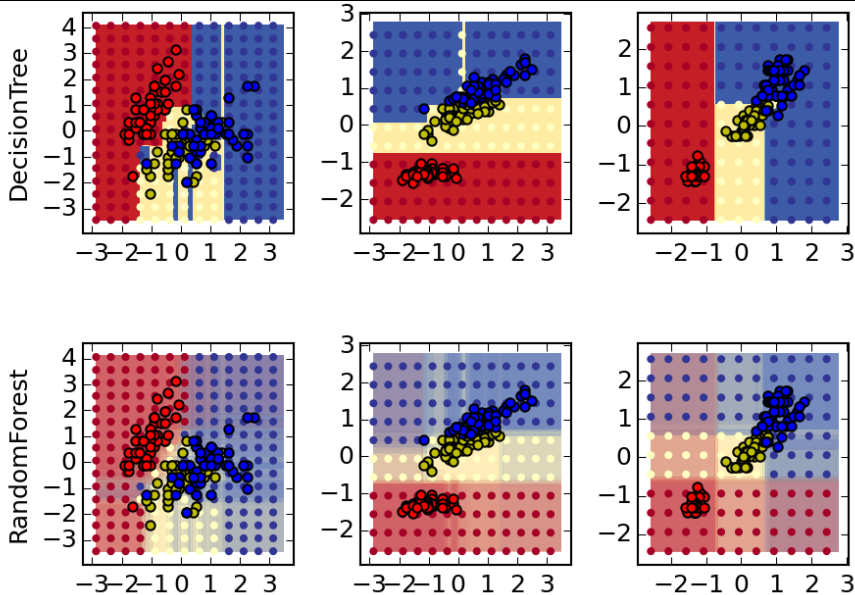
- Fit with a tree of depth 10

staircase of 10 constant values

- Fit a new tree on errors
- Keep going

Boosted regression trees

2 2D intuitions & model averaging



2 Model stacking

$$x \xrightarrow{\text{model}_1} z \xrightarrow{\text{model}_2} y$$

Learn model_1 separately

Directly supervising z :

$z = \hat{y}$ for a (simple) predictive model

Trick: “cross-fit” during training

obtain \hat{y} by splitting the training data

z for a given sample is built

from different samples even in the train set.



Just use `sklearn.ensemble.StackingRegressor`

Useful to assemble non-linear models from simple ones

2 Missing values

Gender	Date Hired	Employee Position Title
M	09/12/1988	Master Police Officer
F	NA	Social Worker IV
M	07/16/2007	Police Officer III
M	01/13/2014	Electrician I
M	04/28/2002	Bus Operator
M	NA	Bus Operator
F	06/26/2006	Social Worker III
F	01/26/2000	Library Assistant I
M	NA 2014	Library Assistant I

2 Classic statistics on missing values

- Model**
- a) a complete data-generating process
 - b) a random process occluding entries

Missing at random situation (MAR)

Theorem [Rubin 1976], if for non-observed values, the probability of missingness does not depend on this non-observed value. maximizing likelihood for observed data while **ignoring** the unobserved values gives maximum likelihood of model a).

MCAR: Missing Completely At Random:

missingness independent of \mathbf{X}

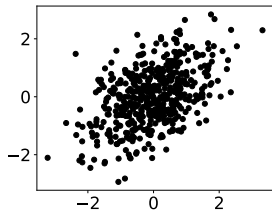
Missing Not at Random situation (MNAR)

Missingness **not ignorable**

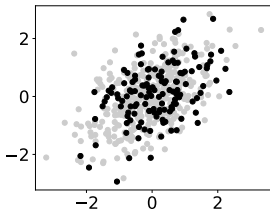
2 Classic statistics on missing values

Model a) a complete data-generating process

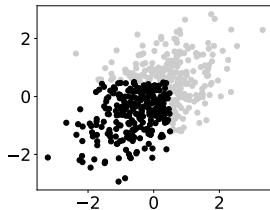
b) a random process occluding entries



Complete



MCAR



MNAR

MCAR: Missing Completely At Random:

missingness independent of **X**

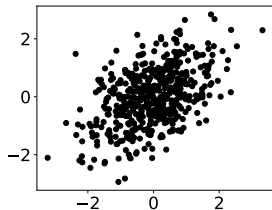
Missing Not at Random situation (MNAR)

Missingness **not** ignorable

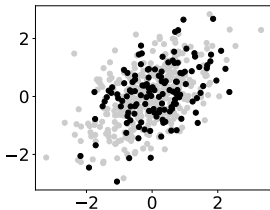
2 Classic statistics on missing values

Model a) a complete data-generating process

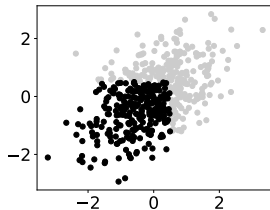
b) a random process occluding entries



Complete



MCAR



MNAR

But

- MAR is not frequent

- Machine learning is not about maximizing likelihoods

Missingness **not** ignorable

2 Classic statistics: Imputation

Fill in information

Gender	Date Hired	Employee Position Title
M	09/12/1988	Master Police Officer
F	NA 2000	Social Worker IV
M	07/16/2007	Police Officer III
M	01/13/2014	Electrician I
M	04/28/2002	Bus Operator
M	NA 2012	Bus Operator
F	06/26/2006	Social Worker III
F	01/26/2000	Library Assistant I
M	NA 2014	Library Assistant I

2 Imputation procedures that work on test set

Mean imputation special case of univariate imputation

Replace NA by the mean of the feature

`sklearn.impute.SimpleImpute`

2 Imputation procedures that work on test set

Mean imputation special case of univariate imputation

Replace NA by the mean of the feature

`sklearn.impute.SimpleImpute`

Conditional imputation

- Modeling one feature as a function of others
- Possible implementation:
iteratively predict one feature as a function of other

`sklearn.impute.IterativeImputer`

Statistics: Conditional imputation considered richer

Machine learning mean imputation can be

detected by non-linear learners

[Josse... 2019]

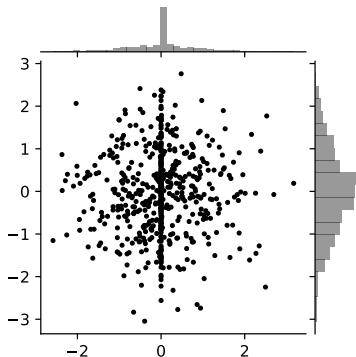
2 Imputation procedures that work on test set

Mean imputation special case of univariate imputation

Replace NA by the mean of the feature

`sklearn.impute.SimpleImpute`

Mean imputation



Conditional imputation

- Modeling one

- Possible imple

iteratively pre

`sklearn.imp`

Statistics: C

Machine lea

detected by non-linear learners

others

tion of other

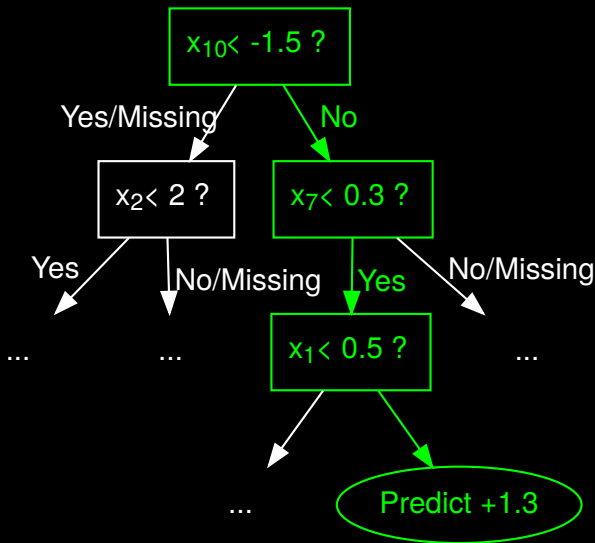
considered richer

can be

[Josse... 2019]

2 Missing attributes inside trees

MIA (Missing Incorporated Attribute) [Josse... 2019]

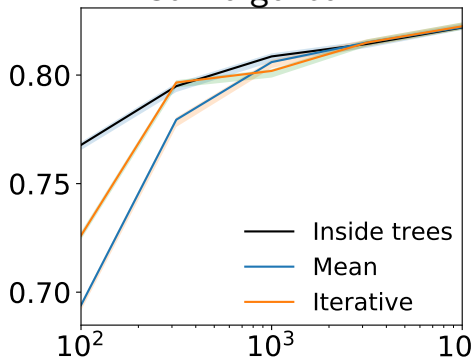


`sklearn.ensemble.HistGradientBoostingClassifier`

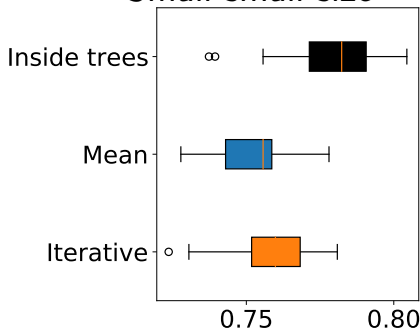
2 Experiments on missing values

Simulation: MCAR + Gradient boosting

Convergence



Small small size



Notebook: [github](#) – @nprost / supervised_missing



2 Imputation is not enough

Pathological case [Josse... 2019]

y depends only on whether data is missing or not

eg tax fraud detection

theory: MNAR = "Missing Not At Random"

 Imputing makes prediction impossible 

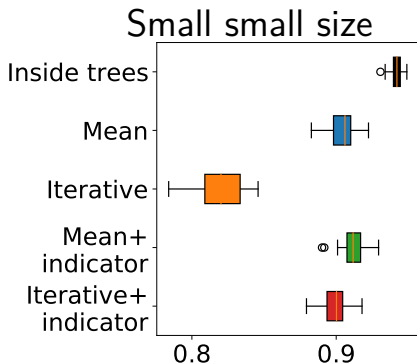
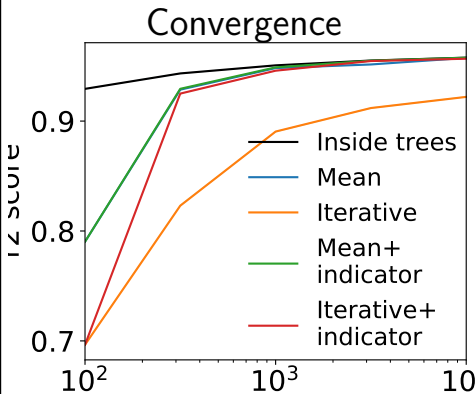
Solution

Add a missingness indicator: extra feature to predict

```
...SimpleImpute(add_indicator=True)  
...IterativeImputer(add_indicator=True)
```

2 Imputation is not enough

Simulation: y depends *indirectly* on missingness
censoring in the data



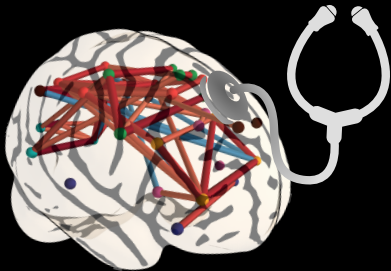
Notebook: github – @nprost / supervised_missing

- Adding a mask is crucial
- Iterative imputation can be detrimental

Recommendations

- High-dimensional settings ($p > 1\,000$):
use linear models
- Lower dimensions, large n ($n > 1\,000$):
use gradient-boosted trees
- Ensembling reduces variance
- Missing values with linear models: iterative imputer
- Missing values with trees: MIA (native support)

3 Advanced learners on brain images



3 Feature clustering to reduce dimension

Challenge: many features

Learn feature groups by clustering

■ Fast clustering for large k

Agglomerative clustering

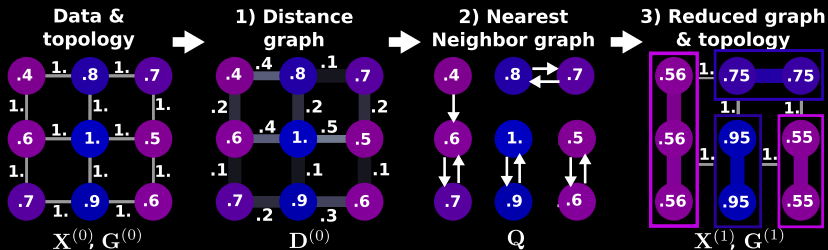


`sklearn.cluster.FeatureAgglomeration`

Choose Ward clustering for best results

[Michel... 2012]

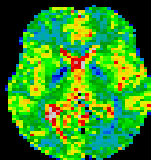
3 ReNA: fast spatial clustering



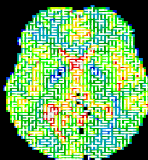
Very fast with spatial constraints

[Hoyos-Ildrobo... 2018a]

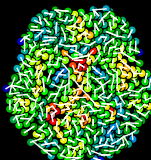
3 ReNA: fast spatial clustering



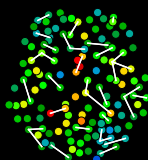
Original



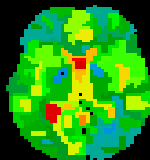
First iteration



Second iteration



Third iteration



Compressed

1. Compute distance on neighborhood graph
2. Assign each vertex to its nearest neighbor on the graph
3. Connect components of graph are next features

Rinse and repeat

`nilearn.regions.Parcellations`

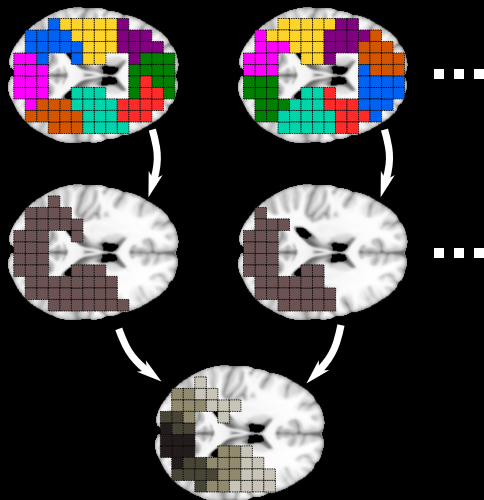
[Hoyos-Ildrobo... 2018a]

3 Fast spatial penalties (FREM)

[Hoyos-Idrobo... 2018b]

- Very fast sub optimal models
- Average many of them

- Very fast sub optimal models
- Average many of them



- Learn parcellation on perturbed data

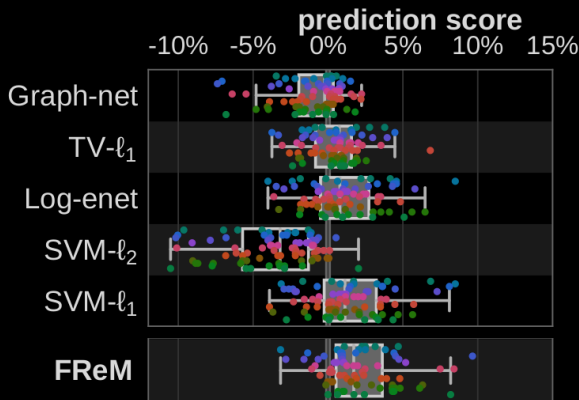
- Estimate linear models

Average the results

3 Fast spatial penalties (FREM)

[Hoyos-Idrobo... 2018b]

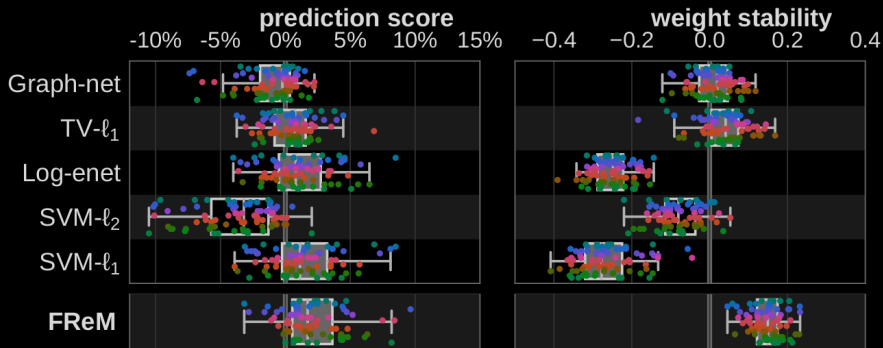
- Very fast sub optimal models
- Average many of them



3 Fast spatial penalties (FREM)

[Hoyos-Idrobo... 2018b]

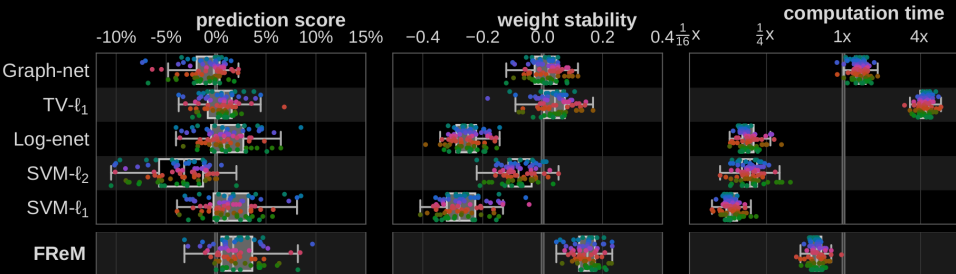
- Very fast sub optimal models
- Average many of them



3 Fast spatial penalties (FREM)

[Hoyos-Idrobo... 2018b]

- Very fast sub optimal models
- Average many of them



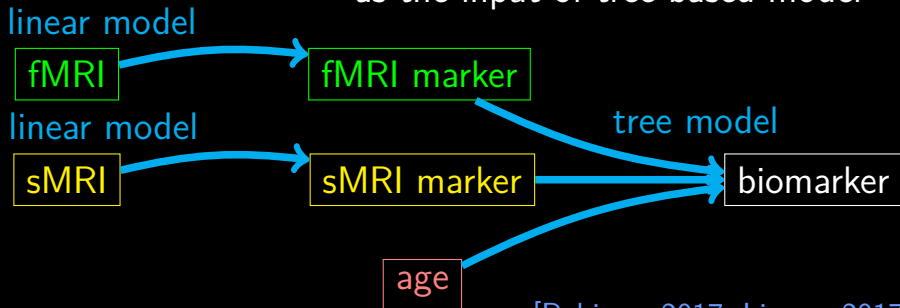
3 Stacking, multimodal non-linear models

Modality-specific linear models

- On each imaging modality fit a linear model

Non-linear model stacking

- Combine the **predicted** outcome values with other clinical variables as the input of tree-based model



[Rahim... 2017, Liem... 2017]

3 Stacking, multimodal non-linear models

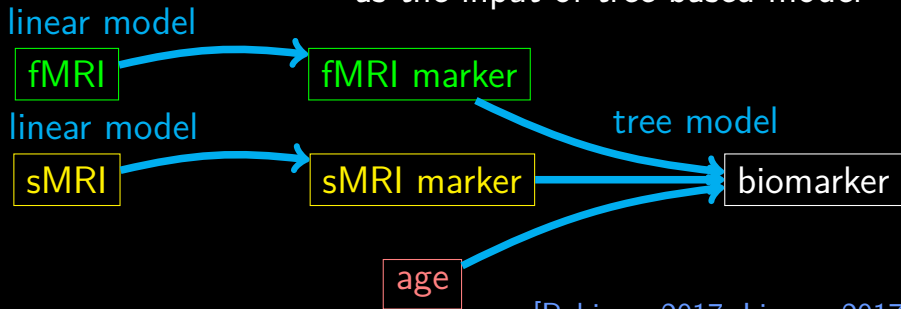
Modality-specific linear models

- On each imaging modality fit a linear model

Non-linear model stacking

- [Engemann... 2020]: missing-value support in trees for subjects with only part of the modalities.

as the input of tree-based model

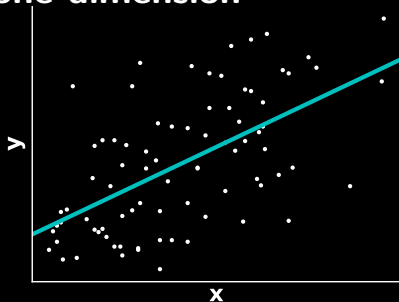


[Rahim... 2017, Liem... 2017]

4 Machine learning principles

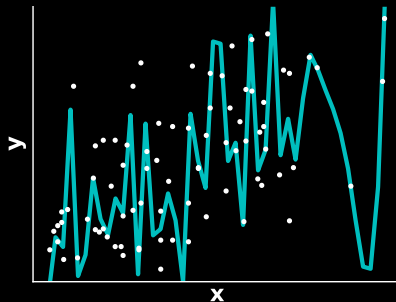
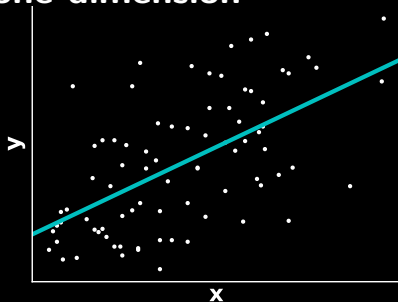
4 Machine learning in a nutshell: regression

A single descriptor:
one dimension



4 Machine learning in a nutshell: regression

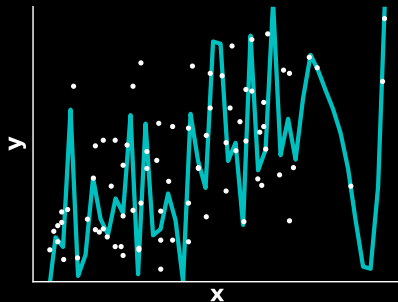
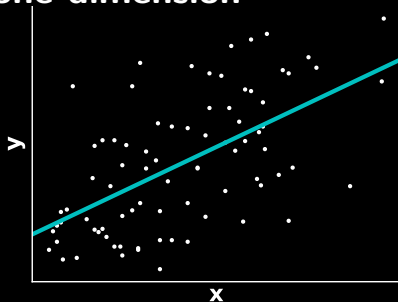
A single descriptor:
one dimension



Which model to prefer?

4 Machine learning in a nutshell: regression

A single descriptor:
one dimension

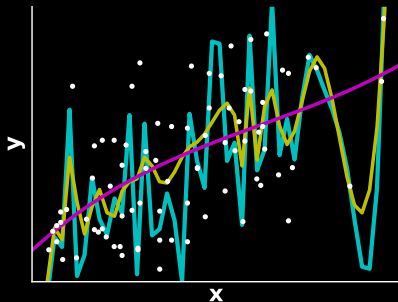
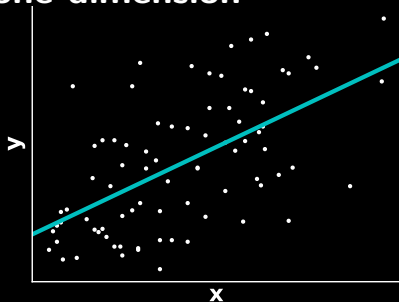


Problem of “*over-fitting*”

- Minimizing error is not always the best strategy (learning noise)
- Test data \neq train data

4 Machine learning in a nutshell: regression

A single descriptor:
one dimension



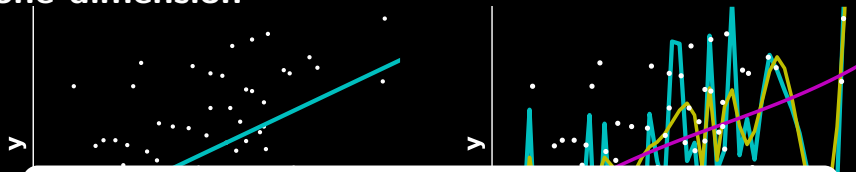
Prefer simple models

= concept of “*regularization*”

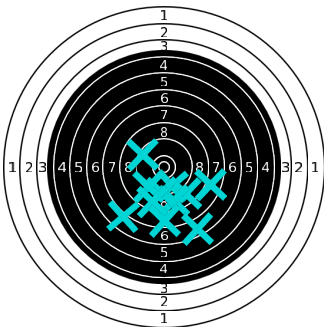
Balance the number of parameters to learn
with the amount of data

4 Machine learning in a nutshell: regression

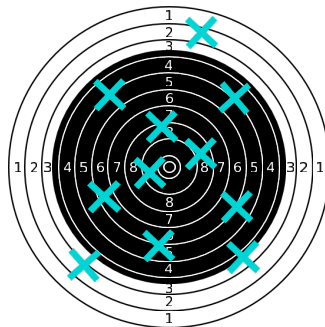
A single descriptor:
one dimension



Bias

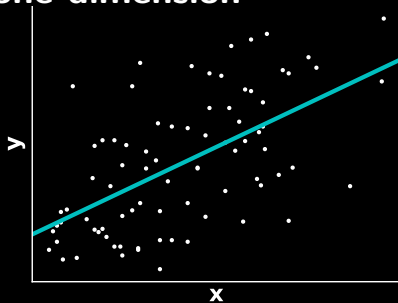


variance tradeoff

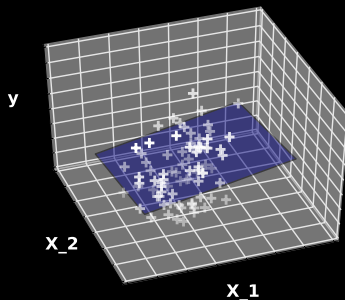


4 Machine learning in a nutshell: regression

A single descriptor:
one dimension



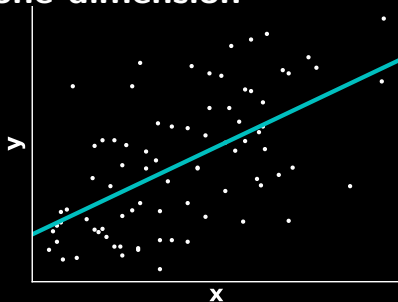
Two descriptors:
2 dimensions



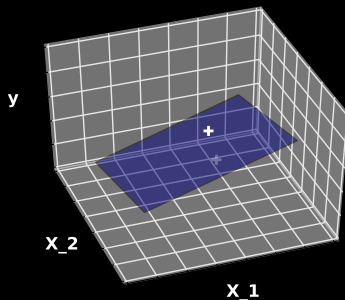
More parameters

4 Machine learning in a nutshell: regression

A single descriptor:
one dimension



Two descriptors:
2 dimensions



More parameters

⇒ Model with more parameters need much more data
“curse of dimensionality”

- Given n pairs $(x, y) \in \mathcal{X} \times \mathcal{Y}$ drawn *i.i.d.*
find a function $f : \mathcal{X} \rightarrow \mathcal{Y}$ such that $f(x) \approx y$

Notation: $\hat{y} \stackrel{\text{def}}{=} f(x)$

- Given n pairs $(x, y) \in \mathcal{X} \times \mathcal{Y}$ drawn *i.i.d.*
find a function $f : \mathcal{X} \rightarrow \mathcal{Y}$ such that $f(x) \approx y$

$$\text{Notation: } \hat{y} \stackrel{\text{def}}{=} f(x)$$

Empirical risk minimization

- Given a “loss” function $l : \mathcal{Y} \times \mathcal{Y} \rightarrow \mathbb{R}$
- Estimation of f :
$$f^* = \operatorname{argmin}_{f \in \mathcal{F}} \mathbb{E}[l(\hat{y}, y)]$$

Can create f such that $\hat{y} = \mathbb{E}[\mathbf{y}|\mathbf{X}]$

- Given n pairs $(x, y) \in \mathcal{X} \times \mathcal{Y}$ drawn *i.i.d.*
find a function $f : \mathcal{X} \rightarrow \mathcal{Y}$ such that $f(x) \approx y$

$$\text{Notation: } \hat{y} \stackrel{\text{def}}{=} f(x)$$

Empirical risk minimization

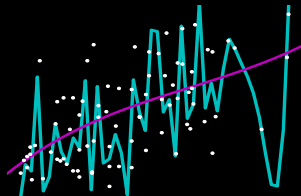
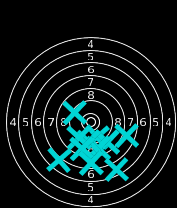
- Given a “loss” function $l : \mathcal{Y} \times \mathcal{Y} \rightarrow \mathbb{R}$
- Estimation of f :
$$f^* = \operatorname{argmin}_{f \in \mathcal{F}} \mathbb{E}[l(\hat{y}, y)]$$

Can create f such that $\hat{y} = \mathbb{E}[\mathbf{y}|\mathbf{X}]$

The inference & control is on f , not parameters

In general, f can be anything (choice of \mathcal{F})

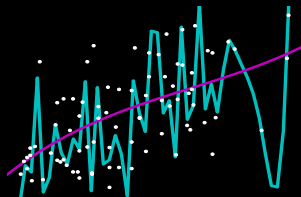
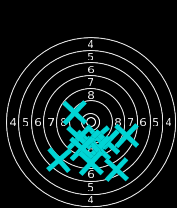
4 Some formalism: bias and regularization



Settings: data (\mathbf{X}, \mathbf{y}) , prediction $\mathbf{y} \sim f(\mathbf{X}, \mathbf{w})$

Our goal: minimize $\|\mathbf{y} - f(\mathbf{X}, \mathbf{w})\|$

4 Some formalism: bias and regularization



Settings: data (\mathbf{X}, \mathbf{y}) , prediction $\mathbf{y} \sim f(\mathbf{X}, \mathbf{w})$

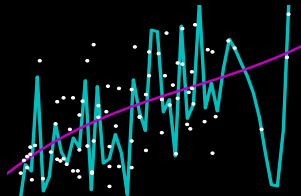
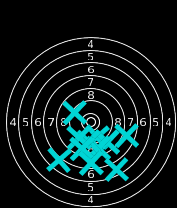
Our goal: minimize $\mathbb{E}[\|\mathbf{y} - f(\mathbf{X}, \mathbf{w})\|]$

We only can measure $\|\mathbf{y} - f(\mathbf{X}, \mathbf{w})\|$

Prediction is very difficult, especially about the future.

Niels Bohr

4 Some formalism: bias and regularization



Settings: data (\mathbf{X}, \mathbf{y}) , prediction $\mathbf{y} \sim f(\mathbf{X}, \mathbf{w})$

Our goal: minimize $\mathbb{E}[\|\mathbf{y} - f(\mathbf{X}, \mathbf{w})\|]$

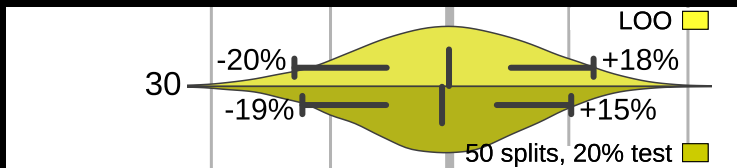
We only can measure $\|\mathbf{y} - f(\mathbf{X}, \mathbf{w})\|$

Solution: bias \mathbf{w} to push toward a plausible solution

In a minimization framework:

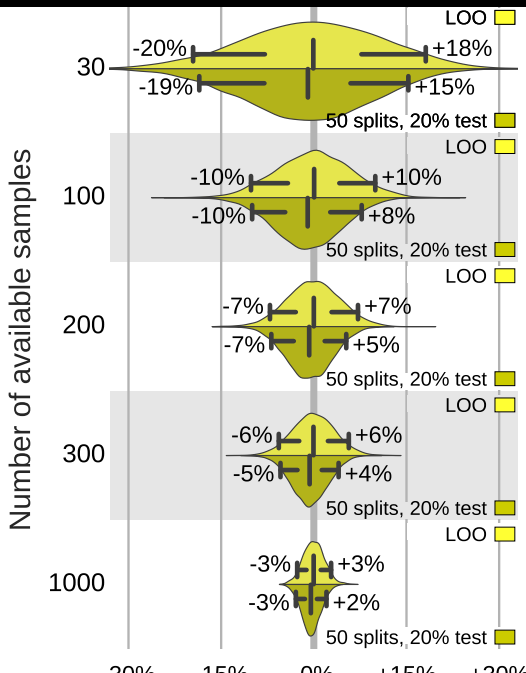
$$\underset{\mathbf{w}}{\text{minimize}} \quad \|\mathbf{y} - f(\mathbf{X}, \mathbf{w})\| + p(\mathbf{w})$$

4 Careful with evidence for generalization



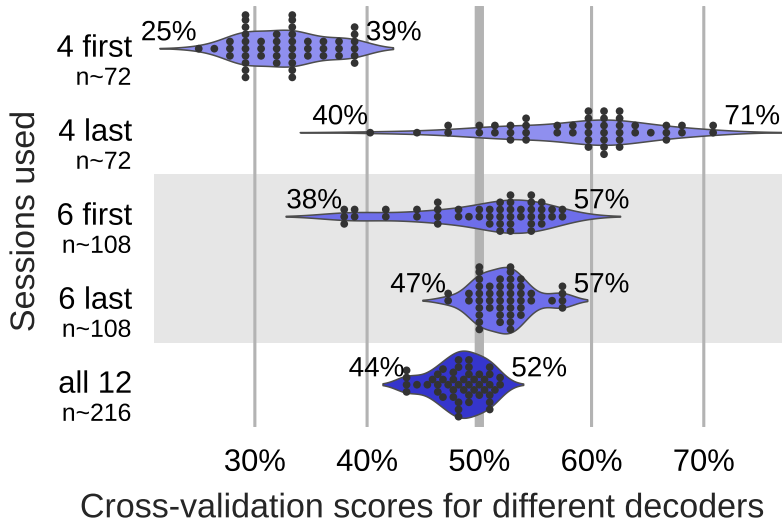
Sampling distribution of test error for $n = 30$

4 Careful with evidence for generalization



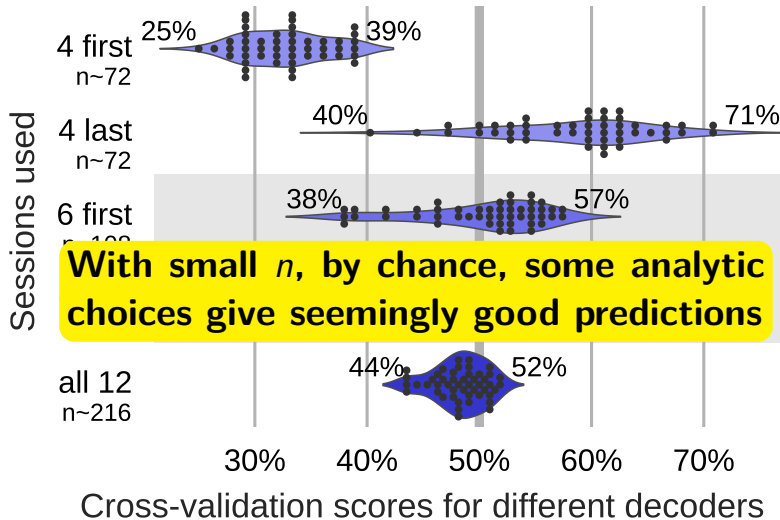
4 Careful with evidence for generalization

Trivial analytic variations on a permuted data:
smoothing, SVM vs log-reg, feature selection



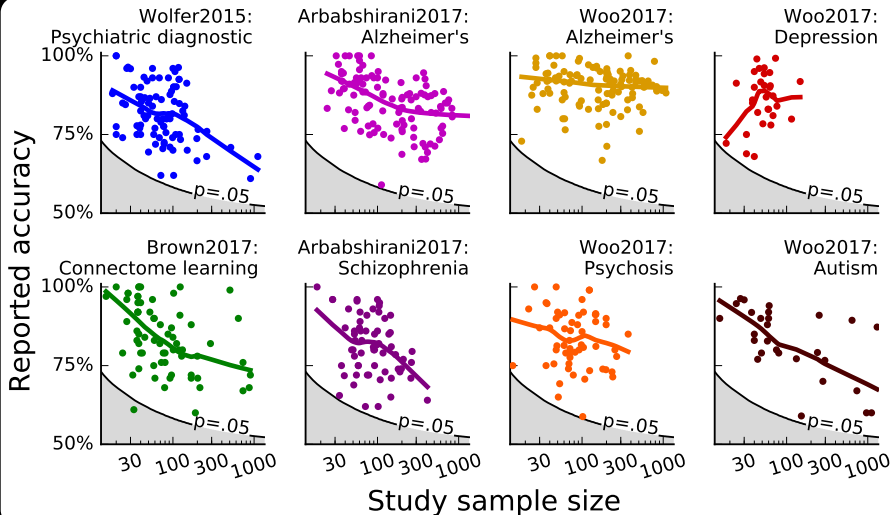
4 Careful with evidence for generalization

Trivial analytic variations on a permuted data:
smoothing, SVM vs log-reg, feature selection



4 Careful with evidence for generalization

In the literature, effect sizes decrease with sample sizes



Going further

- Scipy lecture notes:

<http://www.scipy-lectures.org>

In particular chapter on statistics

- The scikit-learn documentation:

<http://scikit-learn.org>

It's a reference on machine learning

- nilearn

5 References I

- D. A. Engemann, O. Kozynets, D. Sabbagh, G. Lemaitre, G. Varoquaux, F. Liem, and A. Gramfort. Combining electrophysiology with MRI enhances learning of surrogate-biomarkers. *bioRxiv*, 2020. doi: 10.1101/856336. URL <https://www.biorxiv.org/content/early/2019/11/26/856336>.
- A. Hoyos-Idrobo, G. Varoquaux, J. Kahn, and B. Thirion. Recursive nearest agglomeration (rena): fast clustering for approximation of structured signals. *IEEE transactions on pattern analysis and machine intelligence*, 41(3):669–681, 2018a.
- A. Hoyos-Idrobo, G. Varoquaux, Y. Schwartz, and B. Thirion. Frem—scalable and stable decoding with fast regularized ensemble of models. *NeuroImage*, 180:160–172, 2018b.

5 References II

- J. Josse, N. Prost, E. Scornet, and G. Varoquaux. On the consistency of supervised learning with missing values. *arXiv preprint arXiv:1902.06931*, 2019.
- F. Liem, G. Varoquaux, J. Kynast, F. Beyer, S. K. Masouleh, J. M. Huntenburg, L. Lampe, M. Rahim, A. Abraham, R. C. Craddock, ... Predicting brain-age from multimodal imaging data captures cognitive impairment. *NeuroImage*, 2017.
- V. Michel, A. Gramfort, G. Varoquaux, E. Eger, C. Keribin, and B. Thirion. A supervised clustering approach for fMRI-based inference of brain states. *Pattern Recognition*, 45:2041, 2012.
- R. A. Poldrack, G. Huckins, and G. Varoquaux. Establishment of best practices for evidence for prediction: a review. *JAMA psychiatry*, 2019.

5 References III

M. Rahim, B. Thirion, D. Bzdok, I. Buvat, and G. Varoquaux. Joint prediction of multiple scores captures better individual traits from brain images. *Neuroimage*, in rev, 2017.

D. B. Rubin. Inference and missing data. *Biometrika*, 63(3): 581–592, 1976.

G. Varoquaux. Cross-validation failure: small sample sizes lead to large error bars. *NeuroImage*, 2017.