Building meaningful machine learning models for disease prediction

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About me

since 2015 Bioinformatics Postdoc
Next Generation Sequencing
autoinflammatory diseases &
innate immunity

2011 - 2015 PhD in Biology
Is the immune system of plants required to adapt to flowering time change?

2005 - 2011 BSc and MSc of Science in Biology
evolutionary genetics,
immune memory in Drosophila

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Machine Learning (ML) in disease modeling

ML in disease modeling

- tools that can interpret big medical data
- and provide fast, accurate and actionable information
- for precision or personalized medicine

Examples:

- computer-aided diagnosis of breast cancer from mammograms[1]
- identifying signatures of Brain Cancer from MRSI[2]
- identifying gene defects with facial recognition software[3]
- ... and many more ...

[1] Doi 2007.
[2] Sadja 2006.
[3] Levenson 2014.

Image source: Wikimedia Commons

What makes a model meaningful?

Can we trust ML models?

- most ML algorithms model high-degree interactions between variables
- ML models are hard (or impossible) to interpret!
- we often don't know WHY they make decisions
- therefore, it is crucial that our models are meaningful

Image source: Pixabay

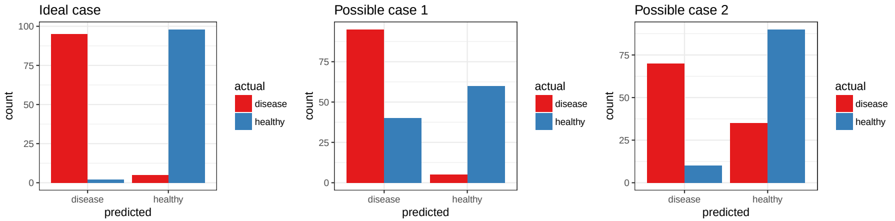
What makes a model meaningful?

- creating ML models is relatively easy
- creating good or meaningful models is hard

Meaningful models

- are generalizable
- answer the question(s) posed...
- ... with sufficient accuracy to be trustworthy

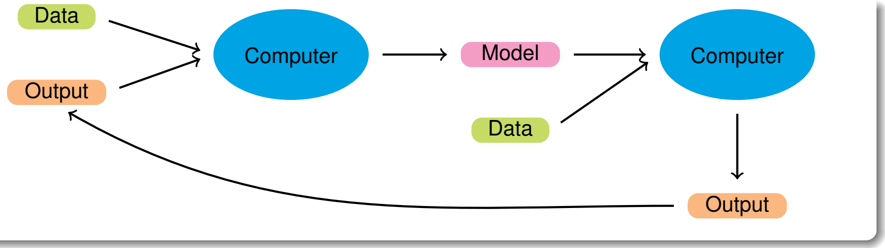
Accuracy depends on the problem!



A quick recap of ML basics

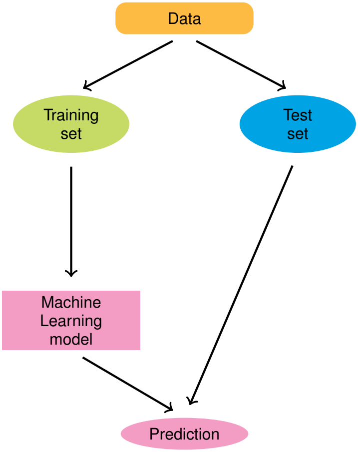
Machine learning

- artificial intelligence (AI)
- data-driven
- algorithms learn by being trained on observed data...
- ... and predict unknown data
- the increase in computational capacity has made ML more accessible

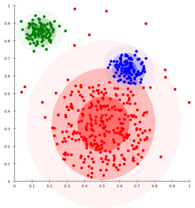


Supervised vs Unsupervised learning

Supervised



Unsupervised



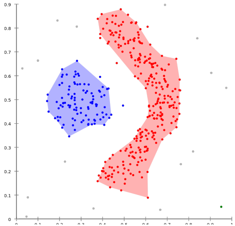
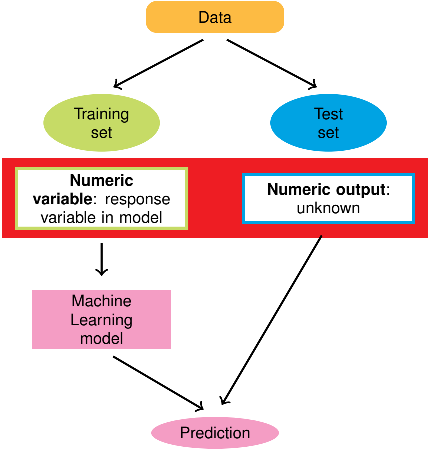


Image Source: Wikipedia

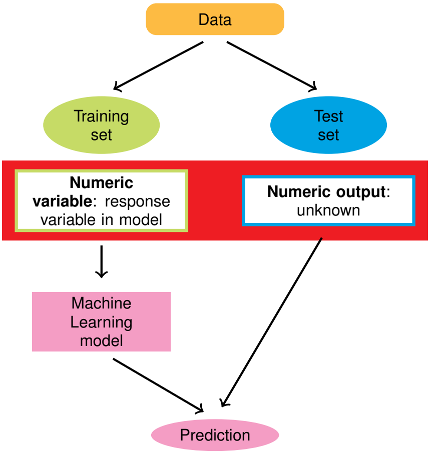
Classification vs Regression

Regression
e.g. weight loss

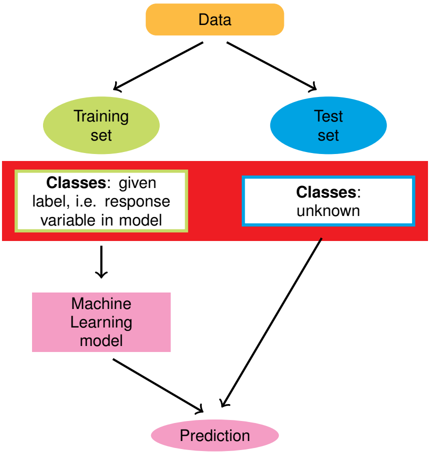


Classification vs Regression

Regression
e.g. weight loss



Classification
e.g. healthy vs disease



Features

- variables used for model training.
- using the right features is crucial.
- More is not necessarily better (overfitting)!
- feature selection
- feature extraction/ engineering

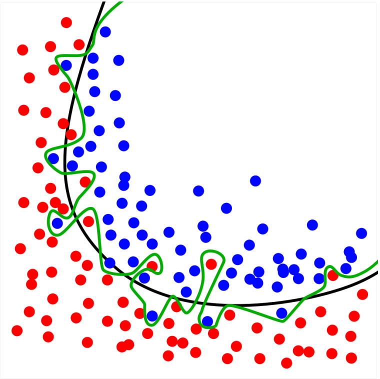
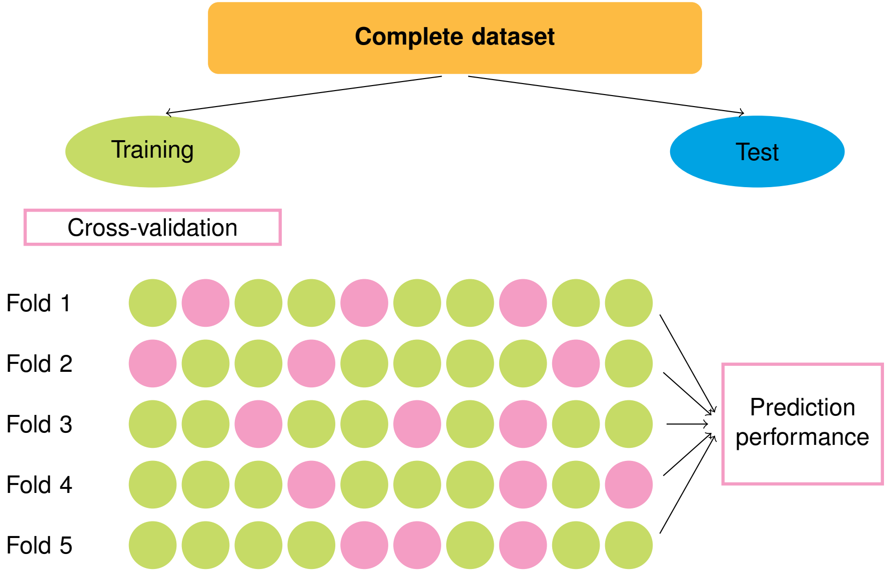


Image Source: Wikipedia

Training, cross-validation and test data

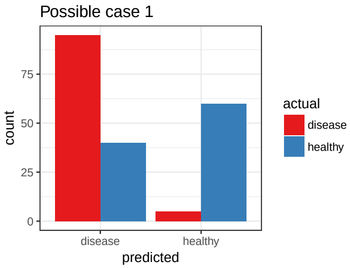


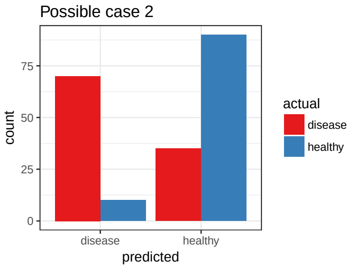
Take home messages:

- ML models learn on observed data
- and predict unknown data

- creating ML models is easy
- creating good models is hard

Meaningful models
- answer specific questions
- are able to generalize to unseen data
- can be trusted





How to build ML models in R

Session setup

- Breast Cancer Wisconsin Dataset[4]

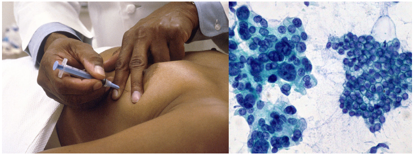


Image Source: Wikipedia

- caret[5]
- h2o[6]

Code will be available on my website and on Github

[4] W. H. Wolberg and O. L. Mangasarian (1990). "Multisurface method of pattern separation for medical diagnosis applied to breast cytology." In: *Proceedings of the National Academy of Sciences* 87.23, pp. 9193–9196.

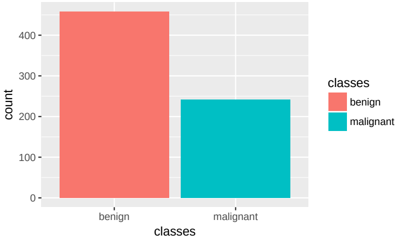
[5] M. Kuhn et al. (2016). *caret: Classification and Regression Training*. R package version 6.0-71.

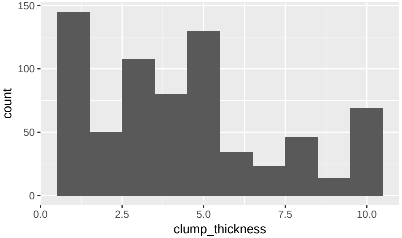
[6] H2O.ai (2017). *h2o: R Interface for H2O*. . R package version 3.10.3.6.

Get to know your data

Response variable

- Is it balanced?



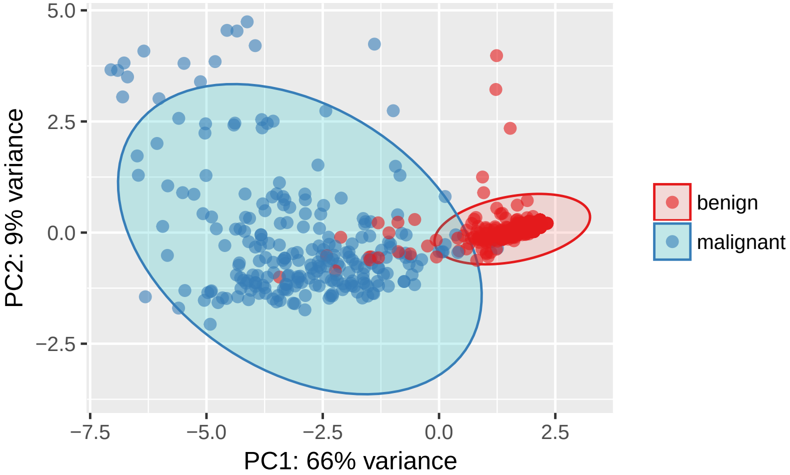


Missing data

- Is there missing data?
- Can we afford to loose data points?
- Or do we use imputation (and introduce additional uncertainty)?

Get to know your data

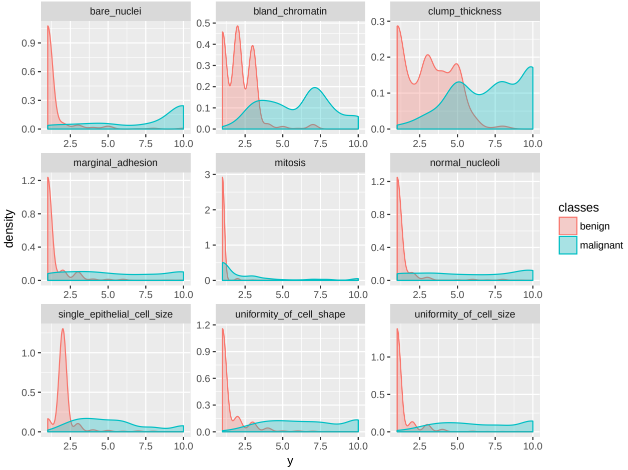
Principal Component Analysis (PCA)



Get to know your data

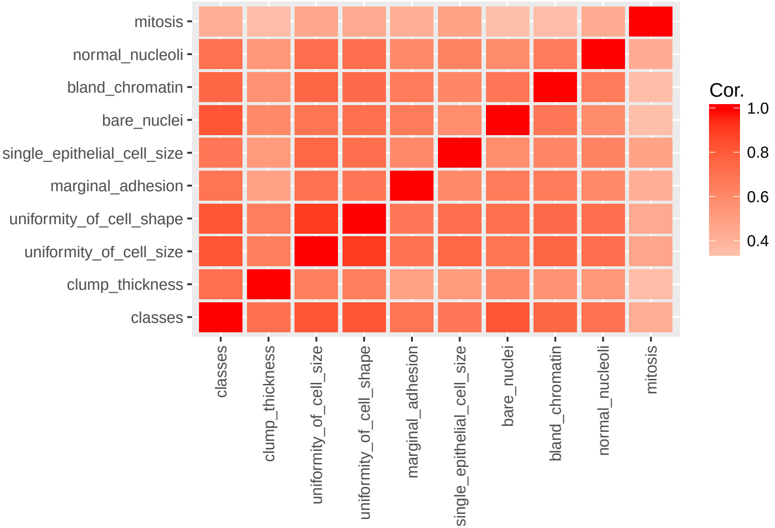
Features

- factors or numeric
- pre-processing



Get to know your data

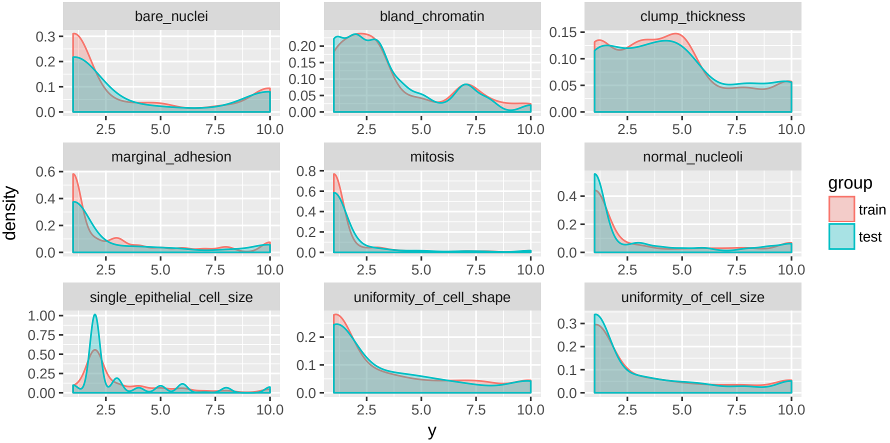
Correlation



Training, validation and test data

Splitting the data into training and test sets - ideally stratified by response class.

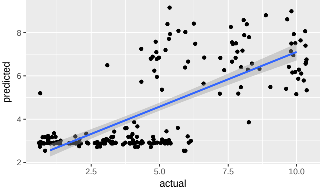
Density distribution



Model examples

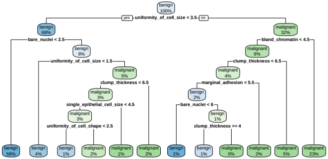
Regression with Linear Models

- e.g. Generalized Linear Models
- with *caret*



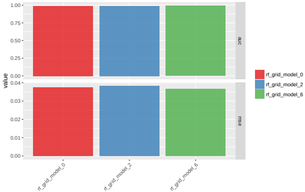
Tree-based classification

- Random Forest or Gradient boosting trees
- with *caret*



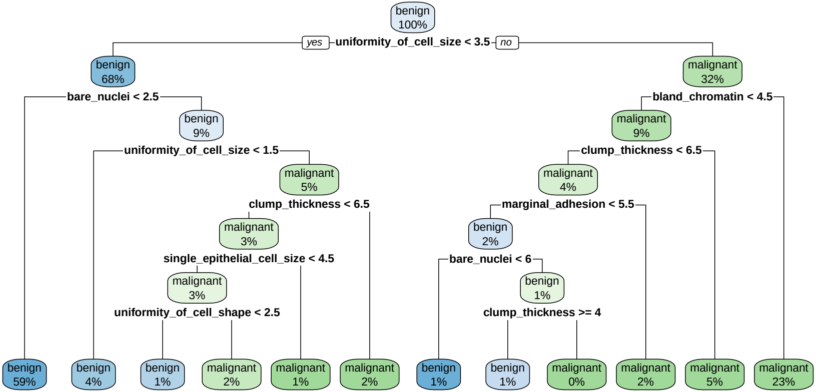
Hyper-parameter tuning

- Grid Search
- with *h2o*

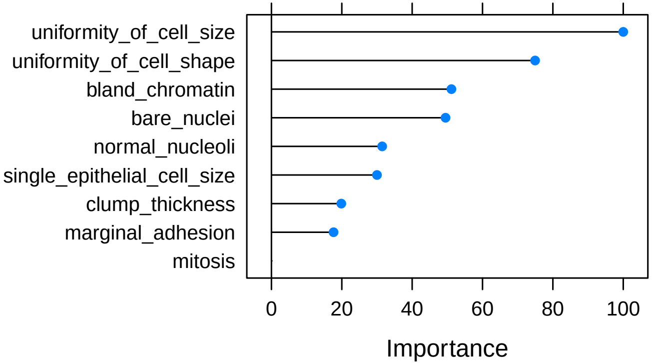


Classification with tree-based models

Decision trees



Feature importance



Evaluating model performance

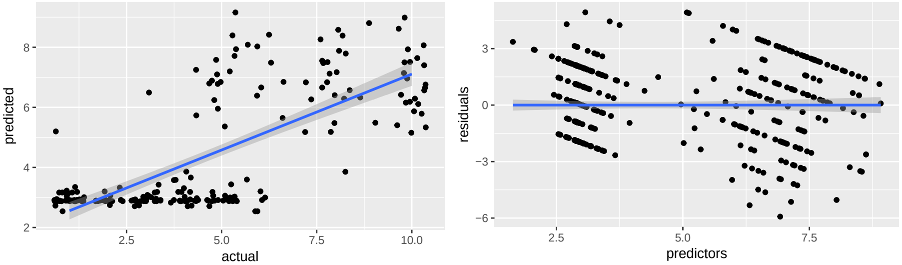
Never use the same data for evaluation that you used for training!

Predictions on test data

Generalized Linear Regression (GLM)

response variable: clump thickness

- RMSE: 1.97
- R^2: 0.50

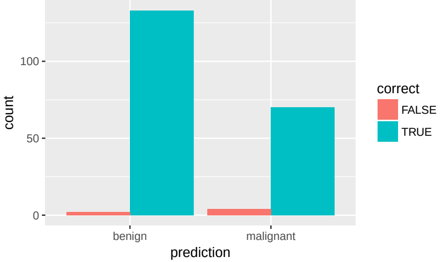


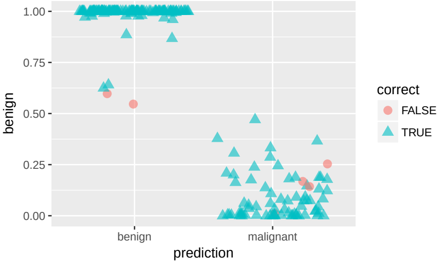
Predictions on test data

Classification with Random Forests

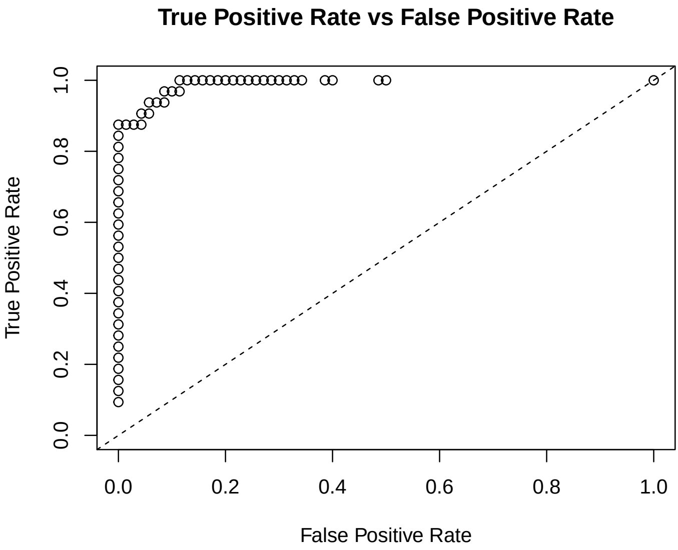
	Reference	
Prediction	benign	malignant
benign	133	2
malignant	4	70

- Recall/ Sensitivity: 0.97
- Specificity: 0.97
- Accuracy: 0.97
- Balanced Accuracy: 0.97





Area Under the Curve (AUC)



Hyper-parameter tuning with grid search

- h2o.grid()
- Random Grid Search (RGS) or Cartesian Grid

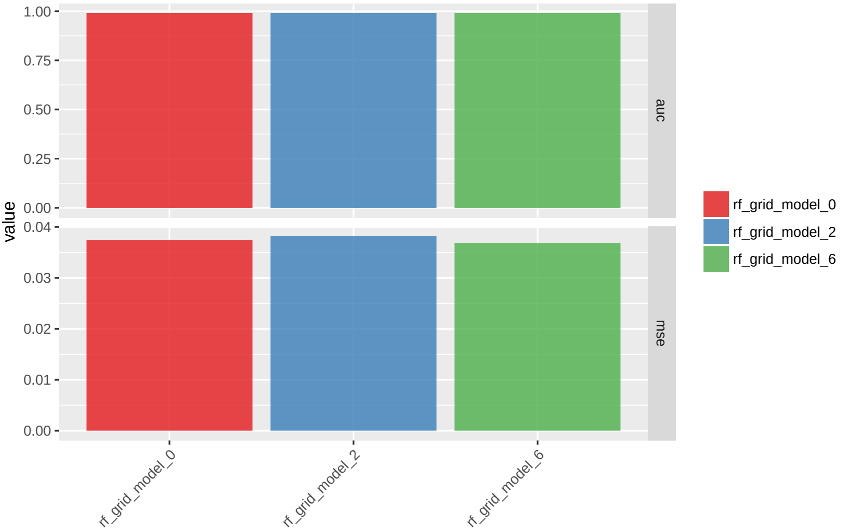
Define a set of hyper-parameters:

- number of trees
- maximum tree depth
- fewest allowed (weighted) observations in a leaf
- etc.

Choose best model from grid:

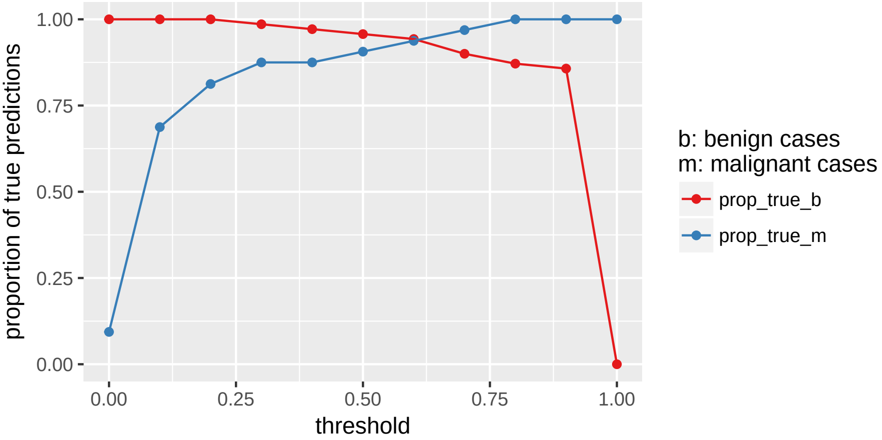
- h2o.getGrid()
- AUC, error, accuracy, etc.

AUC and mean squared error (MSE)

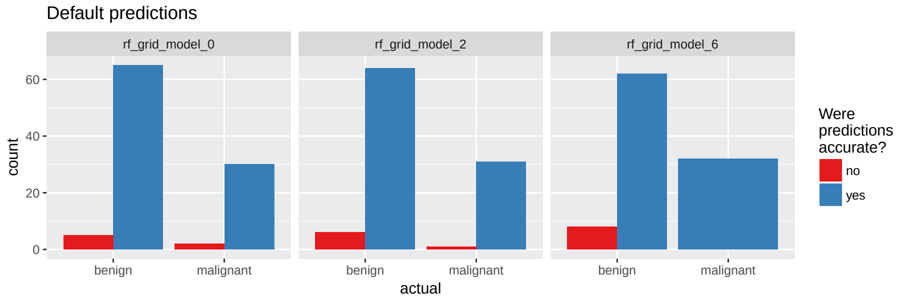


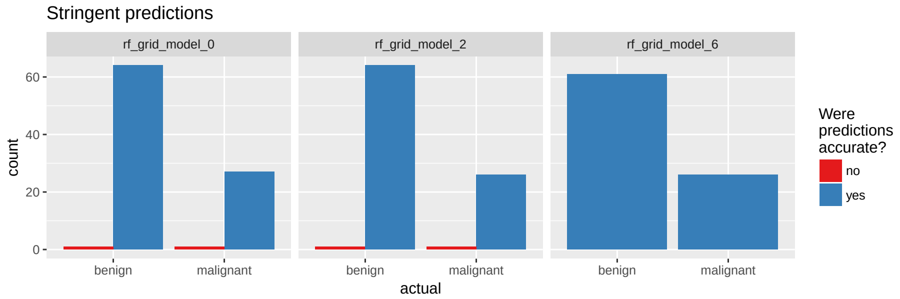
Predictions on test data

Choosing a prediction threshold



Predictions on test data





Take home messages:

- there is no ’one-size-fits-all’ approach to ML
- We want to create meaningful models that we can trust to answer our specific questions!
- know your data well before modeling
- take time to think about pre-processing & features
- test different models & hyper-parameters
- evaluate model performance on independent data
- choose performance measure based on your specific problem
- choose prediction threshold based on your specific problem

Outlook

- ML could make health care more cost-effective by reducing the energy required for interpretation
- 'Big Data' needs to be big!
- the more data, the more accurate the models will be
- for really meaningful models, data needs to be shared
- issues: privacy, platform, quality standards

Thank you for your attention!

Questions?

Slides and code will be available on Github:
https://github.com/ShirinG/Webinar_ISDS

Code will also be on my website:
https://shiring.github.io

You can contact me via
shirin.glander@wwu.de