Building meaningful machine learning models for disease prediction

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Webinar for the ISDS R Group

This document presents the code used to produce the example analysis and figures shown in my webinar on building meaningful machine learning models for disease prediction.

My webinar slides are available on Github

> **Description:** Dr Shirin Glander will go over her work on building machine-learning models to predict the course of different diseases. She will go over building a model, evaluating its performance, and answering or addressing different disease related questions using machine learning. Her talk will cover the theory of machine learning as it is applied using R.

Setup

All analyses are done in R using RStudio. For detailed session information including R version, operating system and package versions, see the `sessionInfo()` output at the end of this document.

All figures are produced with ggplot2.

The dataset

The dataset I am using in these example analyses, is the **Breast Cancer Wisconsin (Diagnostic) Dataset**. The data was downloaded from the UC Irvine Machine Learning Repository.

The first dataset looks at the predictor classes:

- malignant or
- benign breast mass.

The features characterise cell nucleus properties and were generated from image analysis of fine needle aspirates (FNA) of breast masses:

- Sample ID (code number)
- Clump thickness
- Uniformity of cell size
- Uniformity of cell shape
- Marginal adhesion
- Single epithelial cell size
- Number of bare nuclei
- Bland chromatin
- Number of normal nuclei
- Mitosis
- Classes, i.e. diagnosis

```r
bc_data <- read.table("datasets/breast-cancer-wisconsin.data.txt", header = FALSE, sep = ",")
colnames(bc_data) <- c("sample_code_number",
                       "clump_thickness",
                       "uniformity_of_cell_size",
                       "uniformity_of_cell_shape",
                       "marginal_adhesion",
                       "single_epithelial_cell_size",
                       "bare_nuclei",
                       "bland_chromatin",
                       "normal_nucleoli",
                       "mitosis",
                       "classes")

bc_data$classes <- ifelse(bc_data$classes == "2", "benign",
                          ifelse(bc_data$classes == "4", "malignant", NA))
```

Missing data

```r
bc_data[bc_data == "?"] <- NA

# how many NAs are in the data
length(which(is.na(bc_data)))
```

```
## [1] 16
```

```r
# how many samples would we loose, if we removed them?
nrow(bc_data)
```

```
## [1] 699
```

```r
nrow(bc_data[is.na(bc_data), ])
```

```
## [1] 16
```

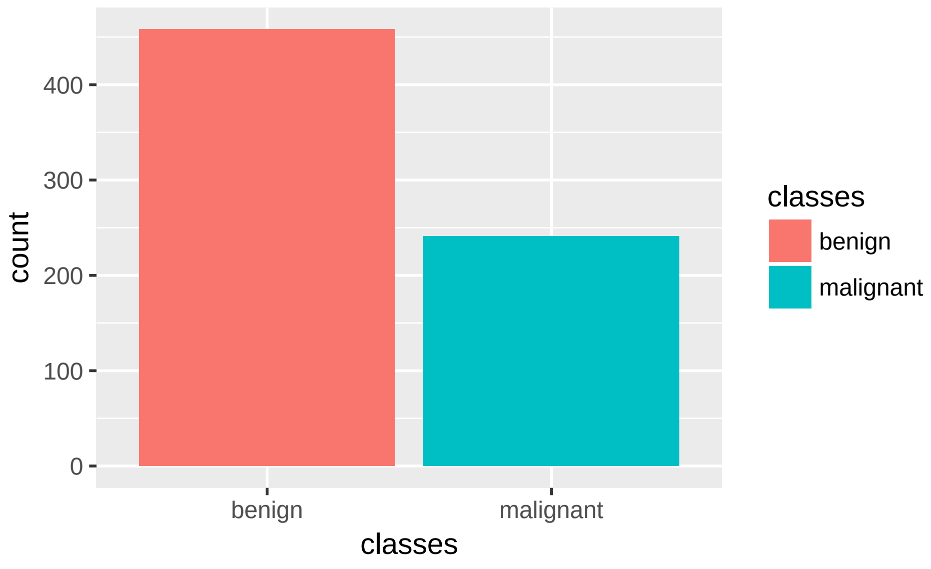
Missing values are imputed with the *mice* package.

```r
# impute missing data
library(mice)

bc_data[,2:10] <- apply(bc_data[, 2:10], 2, function(x) as.numeric(as.character(x)))
dataset_impute <- mice(bc_data[, 2:10],  print = FALSE)
bc_data <- cbind(bc_data[, 11, drop = FALSE], mice::complete(dataset_impute, 1))

bc_data$classes <- as.factor(bc_data$classes)

# how many benign and malignant cases are there?
summary(bc_data$classes)
```

Data exploration

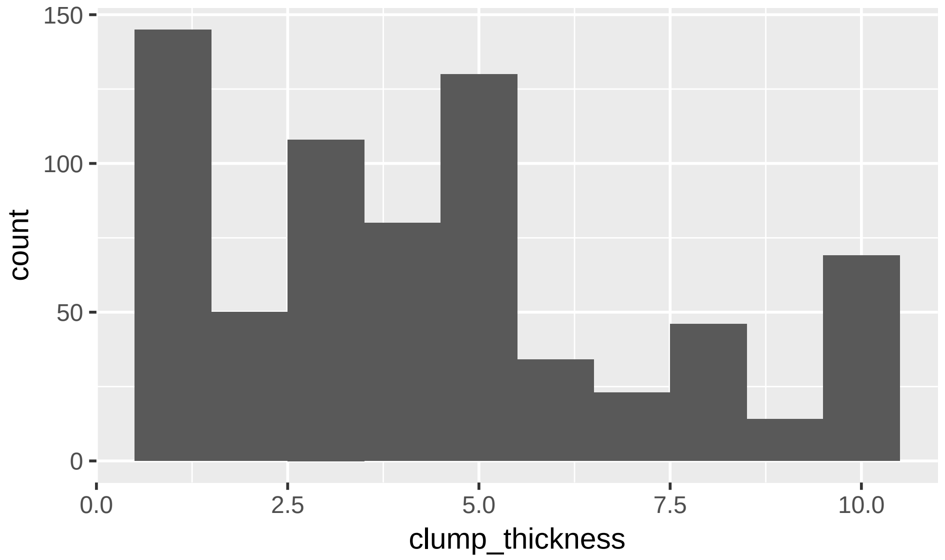
- Response variable for classification

```r
library(ggplot2)

ggplot(bc_data, aes(x = classes, fill = classes)) +
  geom_bar()
```



- Response variable for regression

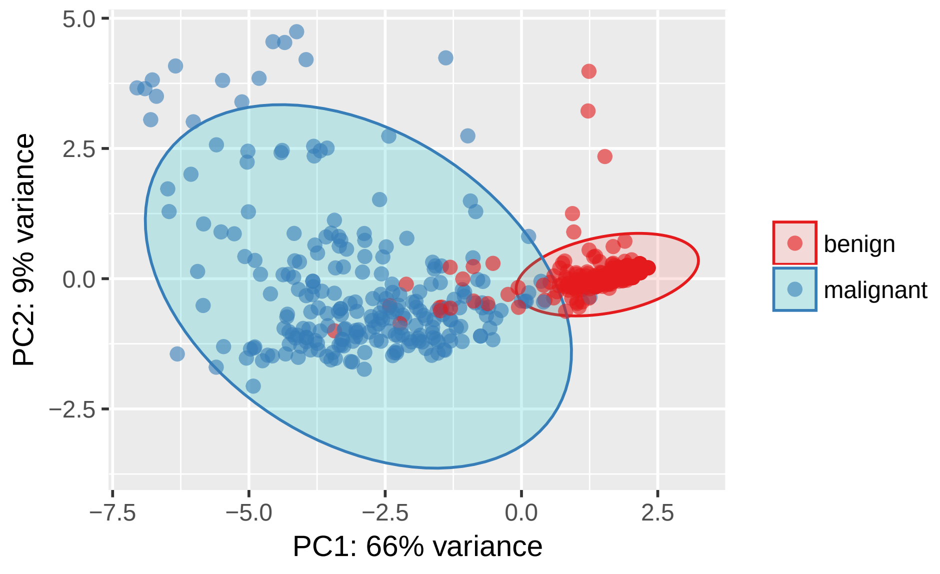
```r
ggplot(bc_data, aes(x = clump_thickness)) +
  geom_histogram(bins = 10)
```



- Principal Component Analysis

```r
library(pcaGoPromoter)
library(ellipse)

# perform pca and extract scores
pcaOutput <- pca(t(bc_data[, -1]), printDropped = FALSE, scale = TRUE, center = TRUE)
pcaOutput2 <- as.data.frame(pcaOutput$scores)

# define groups for plotting
pcaOutput2$groups <- bc_data$classes

centroids <- aggregate(cbind(PC1, PC2) ~ groups, pcaOutput2, mean)
```

```
conf.rgn  <- do.call(rbind, lapply(unique(pcaOutput2$groups), function(t)
  data.frame(groups = as.character(t),
             ellipse(cov(pcaOutput2[pcaOutput2$groups == t, 1:2]),
                   centre = as.matrix(centroids[centroids$groups == t, 2:3]),
                   level = 0.95),
             stringsAsFactors = FALSE)))

ggplot(data = pcaOutput2, aes(x = PC1, y = PC2, group = groups, color = groups)) +
    geom_polygon(data = conf.rgn, aes(fill = groups), alpha = 0.2) +
    geom_point(size = 2, alpha = 0.6) +
    scale_color_brewer(palette = "Set1") +
    labs(color = "",
         fill = "",
         x = paste0("PC1: ", round(pcaOutput$pov[1], digits = 2) * 100, "% variance"),
         y = paste0("PC2: ", round(pcaOutput$pov[2], digits = 2) * 100, "% variance"))
```



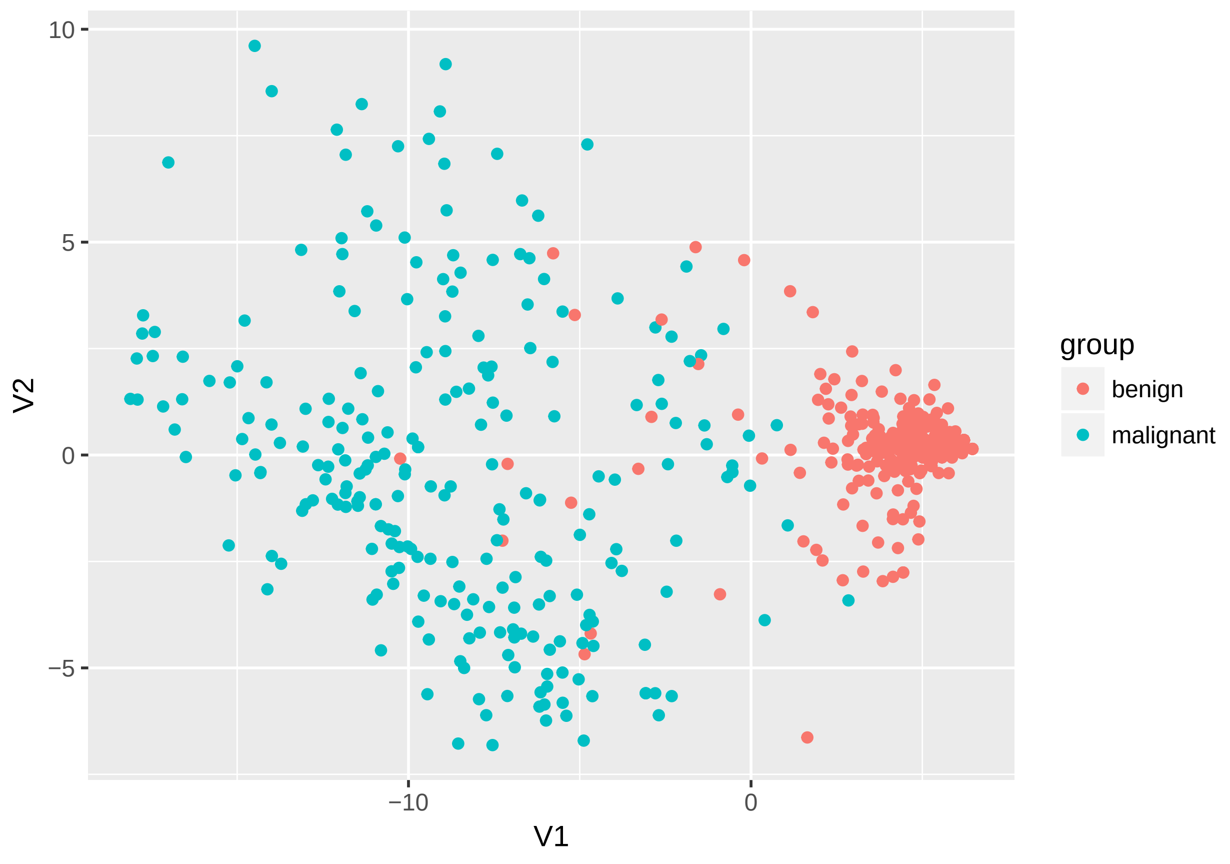
- Multidimensional Scaling

```
library(dplyr)
```

```
##
## Attaching package: 'dplyr'

## The following objects are masked from 'package:Biostrings':
##
##     collapse, intersect, setdiff, setequal, union

## The following object is masked from 'package:XVector':
##
##     slice

## The following objects are masked from 'package:IRanges':
##
##     collapse, desc, intersect, regroup, setdiff, slice, union

## The following objects are masked from 'package:S4Vectors':
##
```

```
##     first, intersect, rename, setdiff, setequal, union

## The following objects are masked from 'package:BiocGenerics':
##
##     combine, intersect, setdiff, union

## The following objects are masked from 'package:stats':
##
##     filter, lag

## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

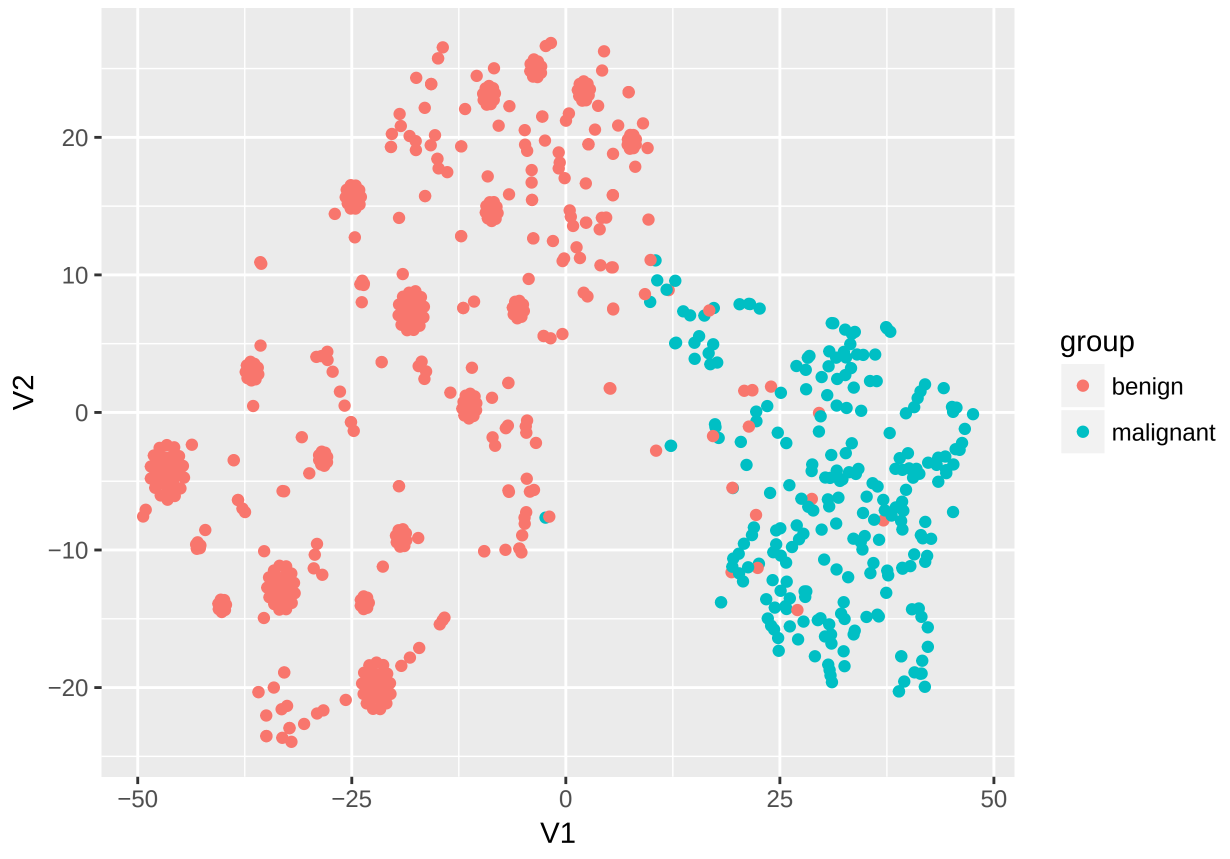
```
select(bc_data, -1) %>%
  dist() %>%
  cmdscale %>%
  as.data.frame() %>%
  mutate(group = bc_data$classes) %>%
  ggplot(aes(x = V1, y = V2, color = group)) +
    geom_point()
```



- t-SNE dimensionality reduction

```
library(tsne)

select(bc_data, -1) %>%
  dist() %>%
  tsne() %>%
  as.data.frame() %>%
  mutate(group = bc_data$classes) %>%
  ggplot(aes(x = V1, y = V2, color = group)) +
    geom_point()
```

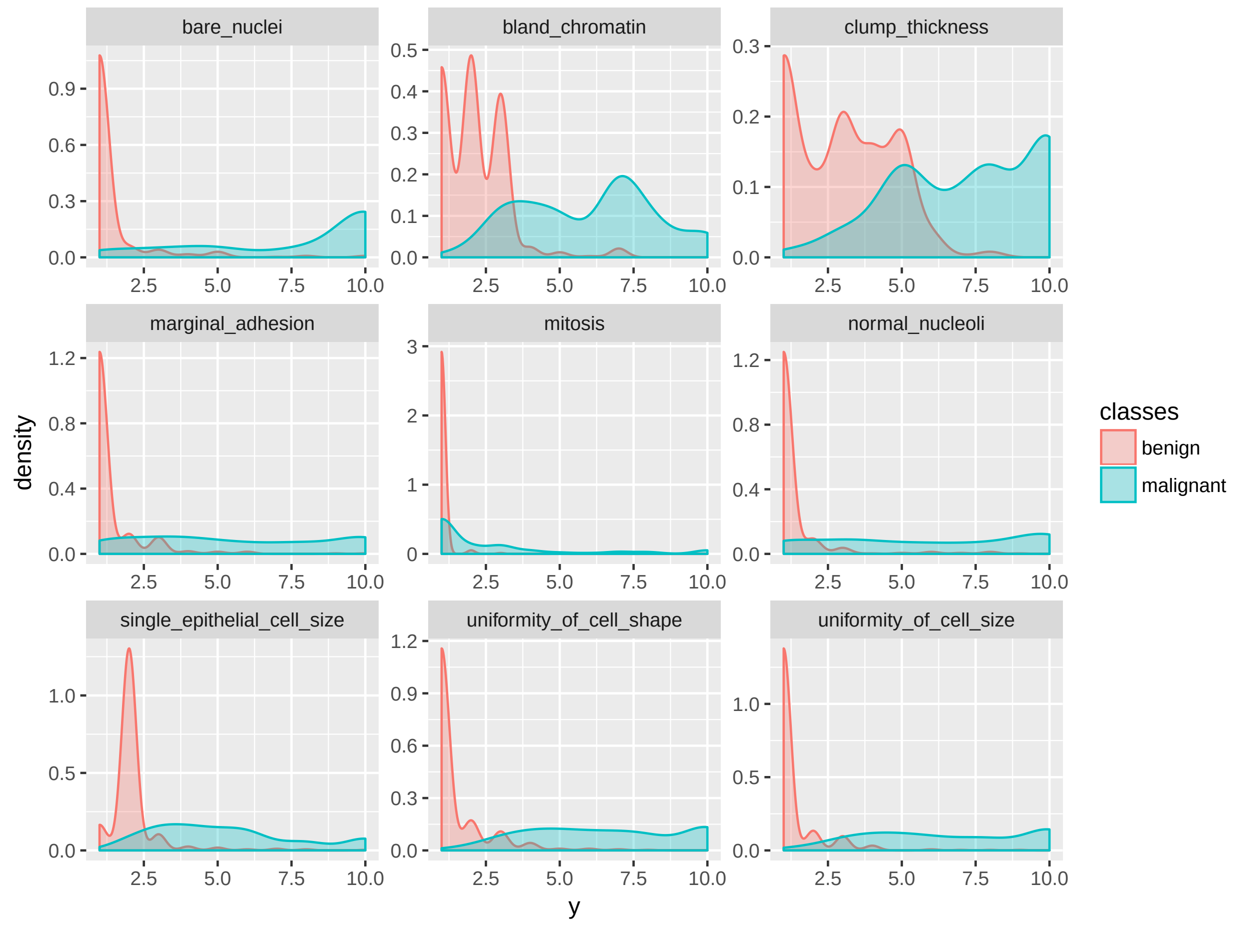
```
## sigma summary: Min. : 0.2945 |1st Qu. : 0.5325 |Median : 0.5978 |Mean : 0.7045 |3rd Qu. : 0.9128 |Ma

## Epoch: Iteration #100 error is: 12.9051118607517

## Epoch: Iteration #200 error is: 0.55100578564023

## Epoch: Iteration #300 error is: 0.507964548605455

## Epoch: Iteration #400 error is: 0.497858645047617

## Epoch: Iteration #500 error is: 0.494929061688897

## Epoch: Iteration #600 error is: 0.493629390821366

## Epoch: Iteration #700 error is: 0.492881739116146

## Epoch: Iteration #800 error is: 0.492432292261577

## Epoch: Iteration #900 error is: 0.492109439434399

## Epoch: Iteration #1000 error is: 0.491872988560014
```



- Features

```
library(tidyr)

gather(bc_data, x, y, clump_thickness:mitosis) %>%
```

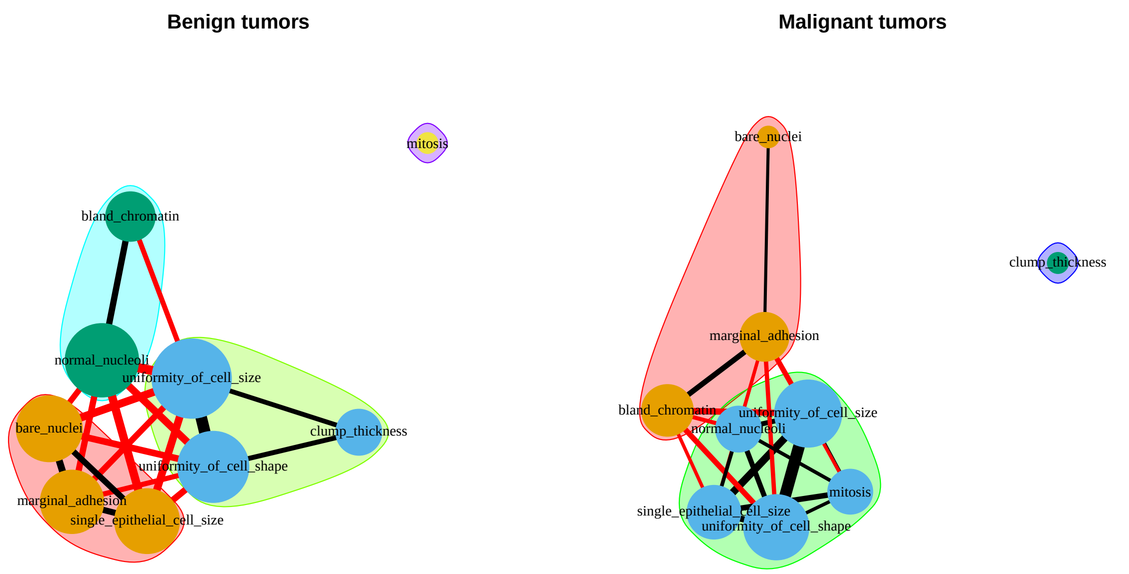
```r
  ggplot(aes(x = y, color = classes, fill = classes)) +
    geom_density(alpha = 0.3) +
    facet_wrap( ~ x, scales = "free", ncol = 3)
```



- Correlation graphs

```r
library(dplyr)
co_mat_benign <- filter(bc_data, classes == "benign") %>%
  select(-1) %>%
  cor()

co_mat_malignant <- filter(bc_data, classes == "malignant") %>%
  select(-1) %>%
  cor()

library(igraph)
g_benign <- graph.adjacency(co_mat_benign,
                         weighted = TRUE,
                         diag = FALSE,
                         mode = "upper")

g_malignant <- graph.adjacency(co_mat_malignant,
                         weighted = TRUE,
                         diag = FALSE,
                          mode = "upper")


# http://kateto.net/networks-r-igraph

cut.off_b <- mean(E(g_benign)$weight)
cut.off_m <- mean(E(g_malignant)$weight)

g_benign_2 <- delete_edges(g_benign, E(g_benign)[weight < cut.off_b])
g_malignant_2 <- delete_edges(g_malignant, E(g_malignant)[weight < cut.off_m])

c_g_benign_2 <- cluster_fast_greedy(g_benign_2)
c_g_malignant_2 <- cluster_fast_greedy(g_malignant_2)
```

```r
par(mfrow=c(1,2))

plot(c_g_benign_2, g_benign_2,
     vertex.size = colSums(co_mat_benign) * 10,
     vertex.frame.color = NA,
     vertex.label.color = "black",
     vertex.label.cex = 0.8,
     edge.width = E(g_benign_2)$weight * 15,
     layout = layout_with_fr(g_benign_2),
     main = "Benign tumors")

plot(c_g_malignant_2, g_malignant_2,
     vertex.size = colSums(co_mat_malignant) * 10,
     vertex.frame.color = NA,
     vertex.label.color = "black",
     vertex.label.cex = 0.8,
     edge.width = E(g_malignant_2)$weight * 15,
     layout = layout_with_fr(g_malignant_2),
     main = "Malignant tumors")
```



Machine Learning packages for R

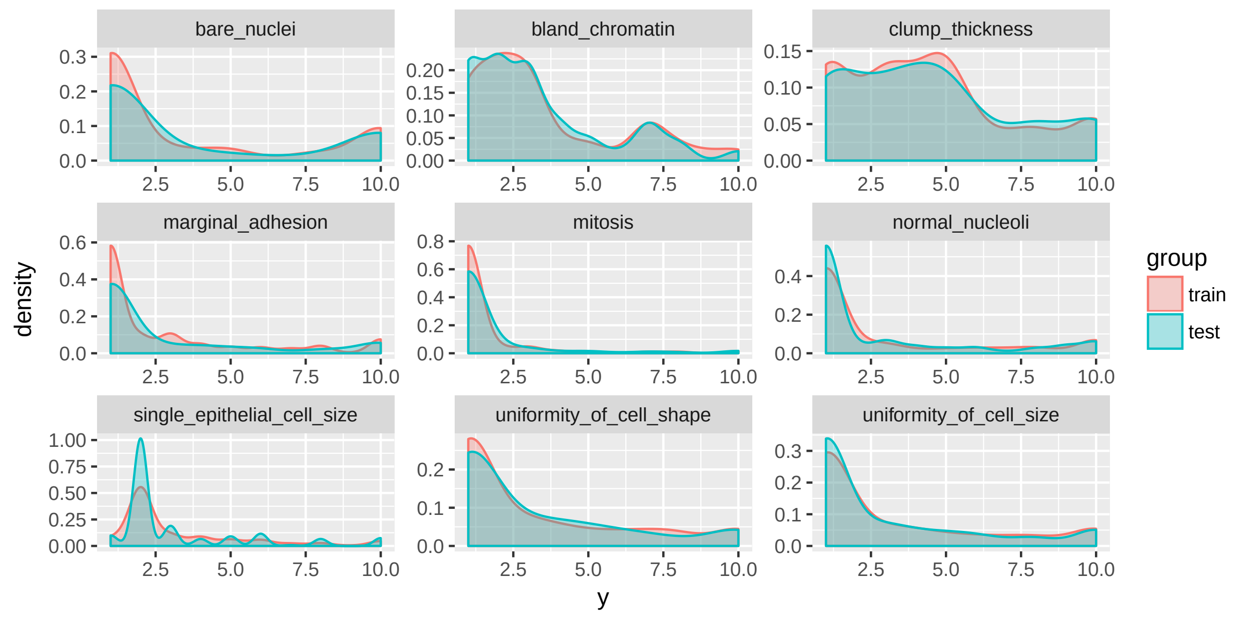
caret

```r
# configure multicore
library(doParallel)
cl <- makeCluster(detectCores())
registerDoParallel(cl)

library(caret)
```

Training, validation and test data

```r
set.seed(42)
index <- createDataPartition(bc_data$classes, p = 0.7, list = FALSE)
train_data <- bc_data[index, ]
test_data  <- bc_data[-index, ]
```

```r
library(dplyr)

rbind(data.frame(group = "train", train_data),
      data.frame(group = "test", test_data)) %>%
  gather(x, y, clump_thickness:mitosis) %>%
  ggplot(aes(x = y, color = group, fill = group)) +
    geom_density(alpha = 0.3) +
    facet_wrap( ~ x, scales = "free", ncol = 3)
```



Regression

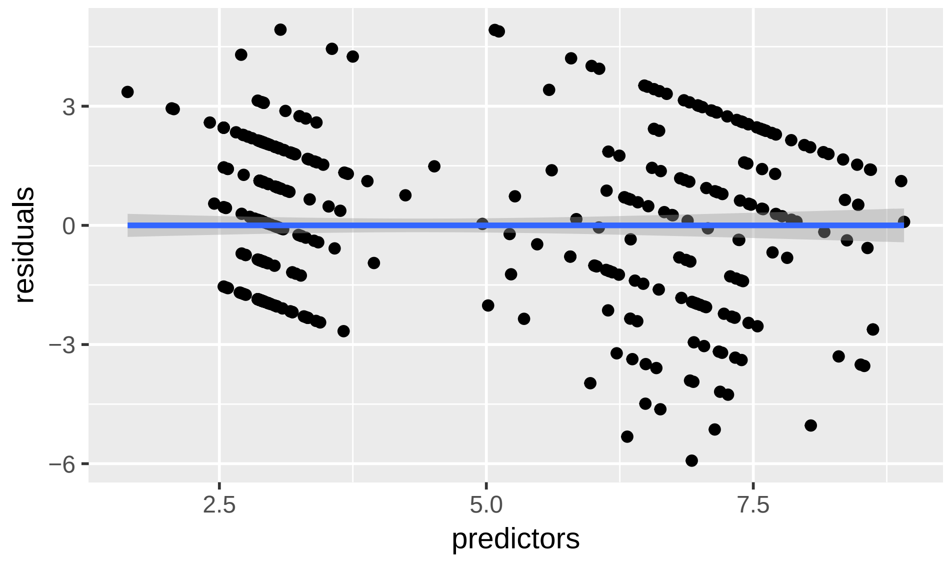
```
set.seed(42)
model_glm <- caret::train(clump_thickness ~ .,
                          data = train_data,
                          method = "glm",
                          preProcess = c("scale", "center"),
                          trControl = trainControl(method = "repeatedcv",
                                                   number = 10,
                                                   repeats = 10,
                                                   savePredictions = TRUE,
                                                   verboseIter = FALSE))
```

```
model_glm
```

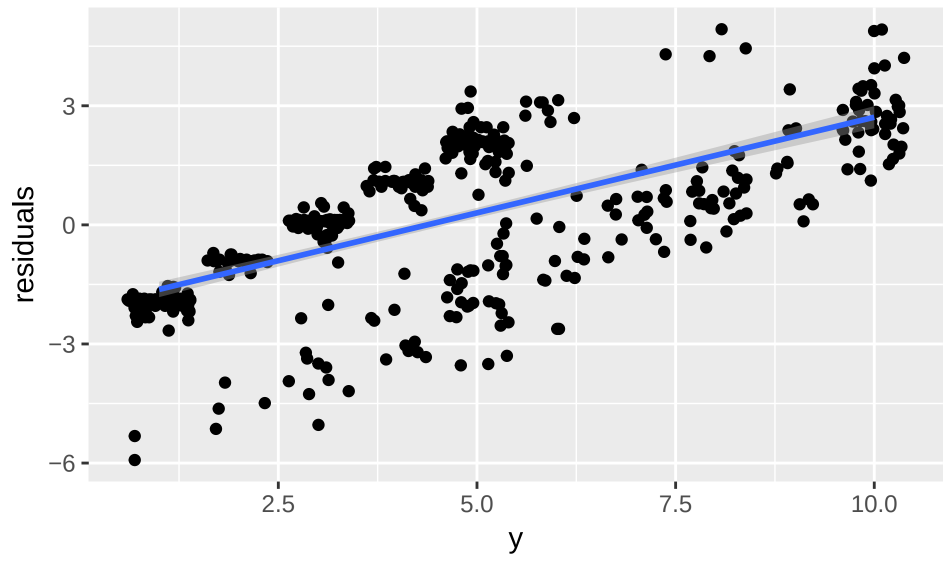
```
## Generalized Linear Model
##
## 490 samples
##   9 predictor
##
## Pre-processing: scaled (9), centered (9)
## Resampling: Cross-Validated (10 fold, repeated 10 times)
## Summary of sample sizes: 441, 441, 440, 442, 441, 440, ...
## Resampling results:
##
##   RMSE      Rsquared
##   1.974296  0.5016141
##
##
```

```
predictions <- predict(model_glm, test_data)
```

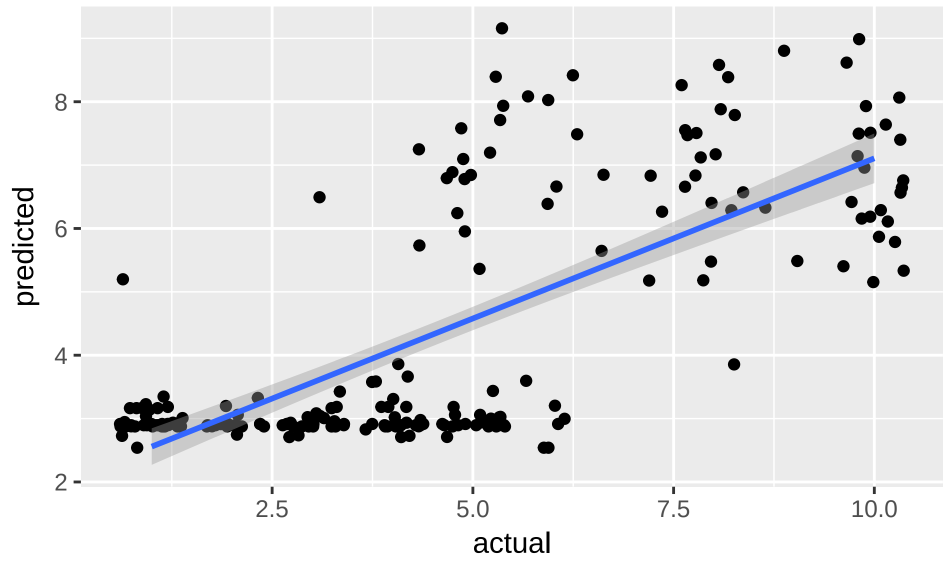
```
# model_glm$finalModel$linear.predictors == model_glm$finalModel$fitted.values
data.frame(residuals = resid(model_glm),
           predictors = model_glm$finalModel$linear.predictors) %>%
  ggplot(aes(x = predictors, y = residuals)) +
    geom_jitter() +
    geom_smooth(method = "lm")
```



```
# y == train_data$clump_thickness
data.frame(residuals = resid(model_glm),
           y = model_glm$finalModel$y) %>%
  ggplot(aes(x = y, y = residuals)) +
    geom_jitter() +
    geom_smooth(method = "lm")
```



```
data.frame(actual = test_data$clump_thickness,
           predicted = predictions) %>%
  ggplot(aes(x = actual, y = predicted)) +
    geom_jitter() +
    geom_smooth(method = "lm")
```

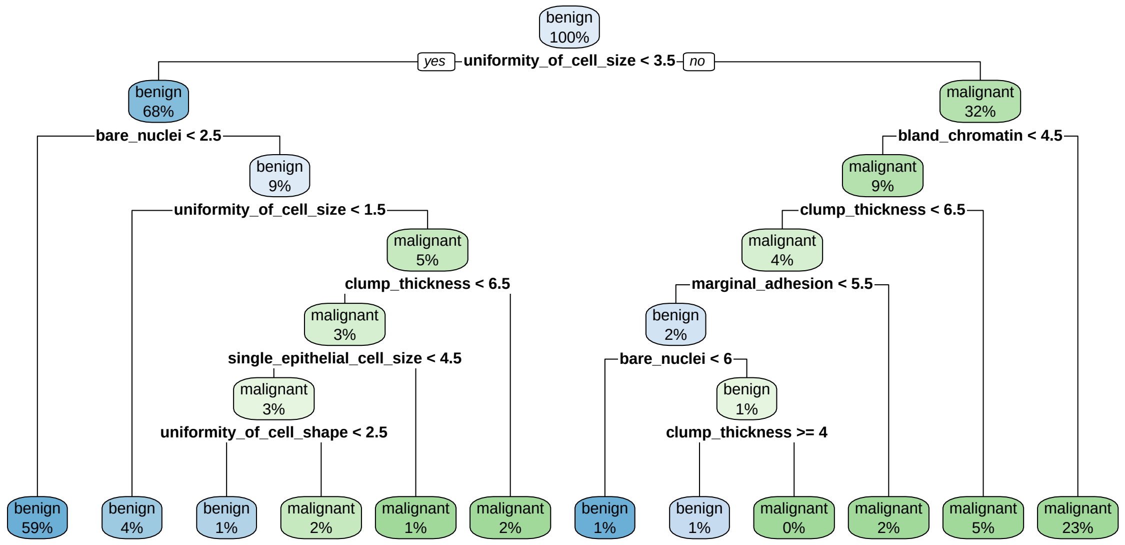


Classification

Decision trees

rpart

```
library(rpart)
library(rpart.plot)

set.seed(42)
fit <- rpart(classes ~ .,
            data = train_data,
            method = "class",
            control = rpart.control(xval = 10,
                                    minbucket = 2,
                                    cp = 0),
             parms = list(split = "information"))

rpart.plot(fit, extra = 100)
```



Random Forests

Random Forests predictions are based on the generation of multiple classification trees. They can be used for both, classification and regression tasks. Here, I show a classification task.

```
set.seed(42)
model_rf <- caret::train(classes ~ .,
                         data = train_data,
                         method = "rf",
                         preProcess = c("scale", "center"),
                         trControl = trainControl(method = "repeatedcv",
                                                  number = 10,
                                                  repeats = 10,
                                                  savePredictions = TRUE,
                                                  verboseIter = FALSE))
```

When you specify `savePredictions = TRUE`, you can access the cross-validation resuls with `model_rf$pred`.

```
model_rf$finalModel$confusion
```

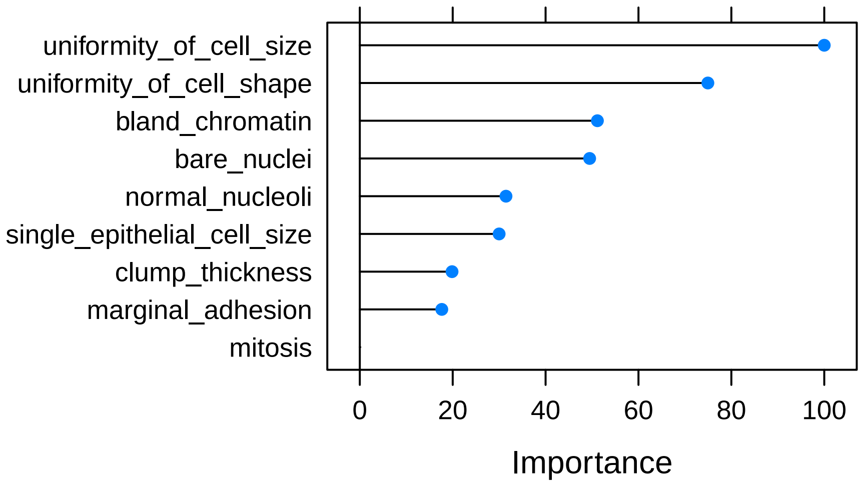
```
##           benign malignant class.error
## benign       313         8  0.02492212
## malignant      4       165  0.02366864
```

- Feature Importance

```
imp <- model_rf$finalModel$importance
imp[order(imp, decreasing = TRUE), ]
```

```
##     uniformity_of_cell_size    uniformity_of_cell_shape
##                   54.416003                   41.553022
##             bland_chromatin                 bare_nuclei
##                   29.343027                   28.483842
##             normal_nucleoli single_epithelial_cell_size
##                   19.239635                   18.480155
##             clump_thickness           marginal_adhesion
##                   13.276702                   12.143355
##                     mitosis
##                    3.081635
```

```
# estimate variable importance
importance <- varImp(model_rf, scale = TRUE)
plot(importance)
```



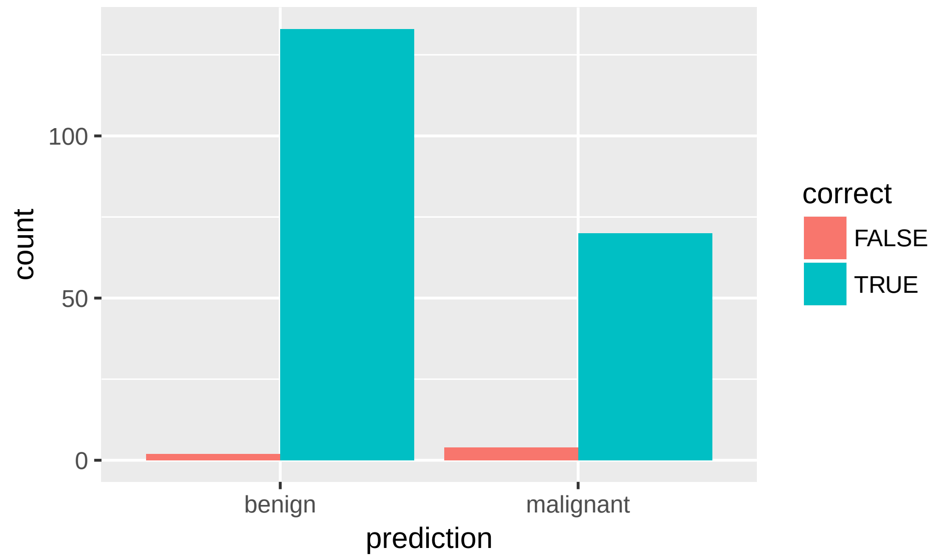
- predicting test data

```
confusionMatrix(predict(model_rf, test_data), test_data$classes)
```

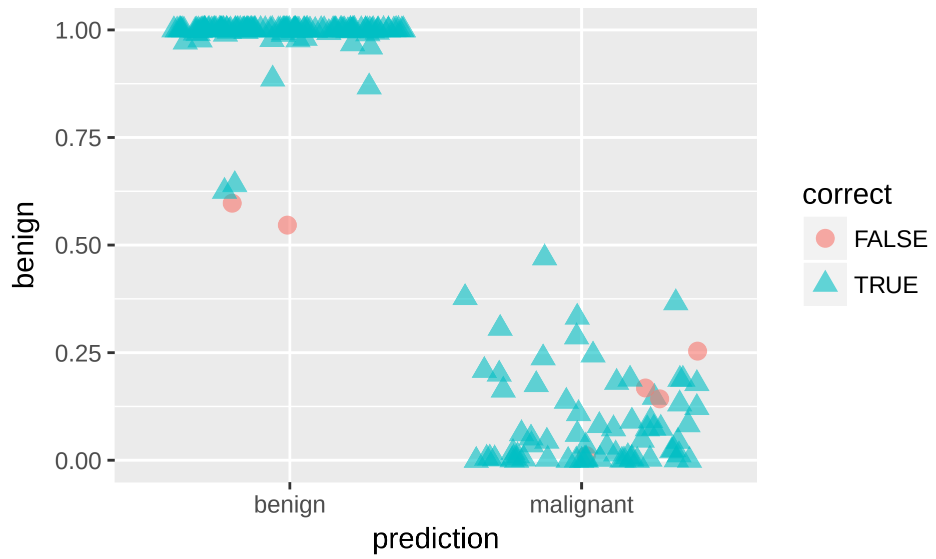
```
## Confusion Matrix and Statistics
##
##            Reference
## Prediction  benign malignant
##   benign       133         2
##   malignant      4        70
##
##                Accuracy : 0.9713
##                  95% CI : (0.9386, 0.9894)
##     No Information Rate : 0.6555
##     P-Value [Acc > NIR] : <2e-16
##
##                   Kappa : 0.9369
##  Mcnemar's Test P-Value : 0.6831
##
##             Sensitivity : 0.9708
##             Specificity : 0.9722
##          Pos Pred Value : 0.9852
##          Neg Pred Value : 0.9459
##              Prevalence : 0.6555
##          Detection Rate : 0.6364
##    Detection Prevalence : 0.6459
##       Balanced Accuracy : 0.9715
##
```

```
##         'Positive' Class : benign
##
```

```
results <- data.frame(actual = test_data$classes,
                      predict(model_rf, test_data, type = "prob"))

results$prediction <- ifelse(results$benign > 0.5, "benign",
                             ifelse(results$malignant > 0.5, "malignant", NA))

results$correct <- ifelse(results$actual == results$prediction, TRUE, FALSE)

ggplot(results, aes(x = prediction, fill = correct)) +
  geom_bar(position = "dodge")
```



```
ggplot(results, aes(x = prediction, y = benign, color = correct, shape = correct)) +
  geom_jitter(size = 3, alpha = 0.6)
```



Extreme gradient boosting trees

Extreme gradient boosting (XGBoost) is a faster and improved implementation of gradient boosting for supervised learning.

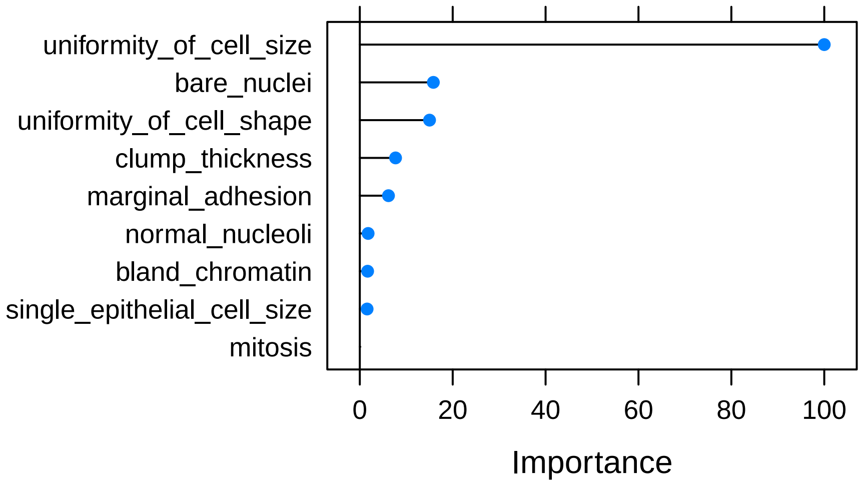
> "XGBoost uses a more regularized model formalization to control over-fitting, which gives it better performance." Tianqi Chen, developer of xgboost

XGBoost is a tree ensemble model, which means the sum of predictions from a set of classification and regression trees (CART). In that, XGBoost is similar to Random Forests but it uses a different approach to model training. Can be used for classification and regression tasks. Here, I show a classification task.

```
set.seed(42)
model_xgb <- caret::train(classes ~ .,
                          data = train_data,
                          method = "xgbTree",
                          preProcess = c("scale", "center"),
                          trControl = trainControl(method = "repeatedcv",
                                                   number = 10,
                                                   repeats = 10,
                                                   savePredictions = TRUE,
                                                   verboseIter = FALSE))
```

- Feature Importance

```
importance <- varImp(model_xgb, scale = TRUE)
plot(importance)
```



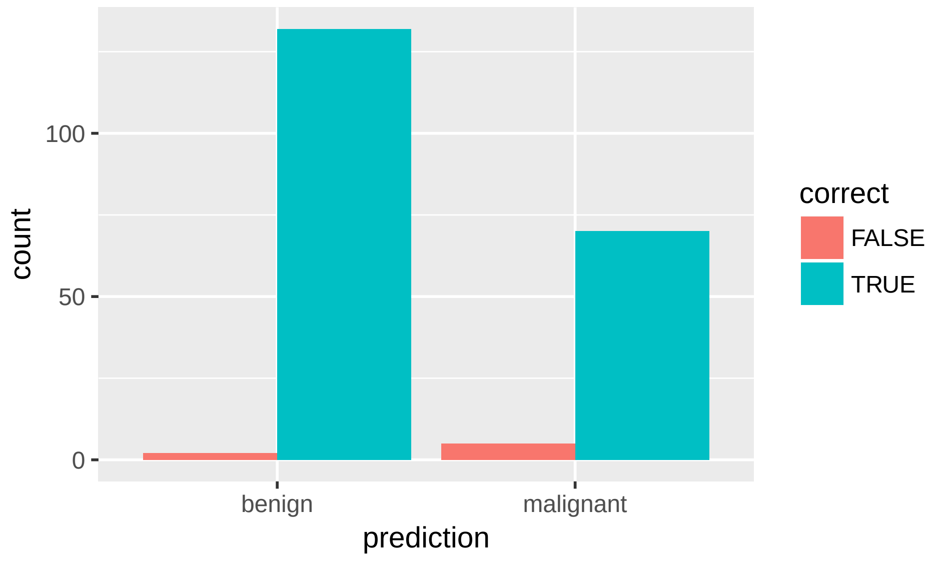
- predicting test data

```
confusionMatrix(predict(model_xgb, test_data), test_data$classes)
```

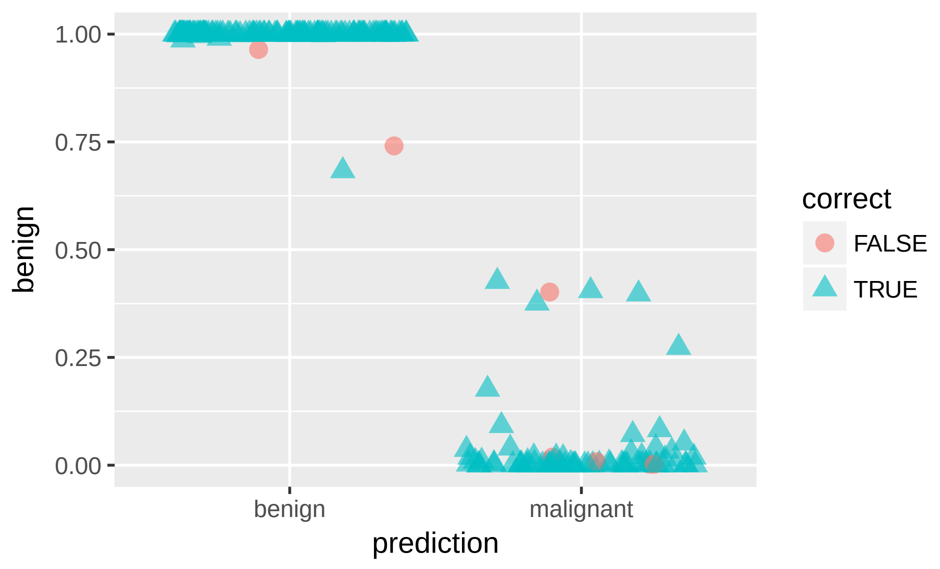
```
## Confusion Matrix and Statistics
##
##            Reference
## Prediction  benign malignant
##   benign       132         2
##   malignant      5        70
##
```

```
##                Accuracy : 0.9665
##                  95% CI : (0.9322, 0.9864)
##     No Information Rate : 0.6555
##     P-Value [Acc > NIR] : <2e-16
##
##                   Kappa : 0.9266
##  Mcnemar's Test P-Value : 0.4497
##
##             Sensitivity : 0.9635
##             Specificity : 0.9722
##          Pos Pred Value : 0.9851
##          Neg Pred Value : 0.9333
##              Prevalence : 0.6555
##          Detection Rate : 0.6316
##    Detection Prevalence : 0.6411
##       Balanced Accuracy : 0.9679
##
##        'Positive' Class : benign
##
```

```
results <- data.frame(actual = test_data$classes,
                      predict(model_xgb, test_data, type = "prob"))

results$prediction <- ifelse(results$benign > 0.5, "benign",
                             ifelse(results$malignant > 0.5, "malignant", NA))

results$correct <- ifelse(results$actual == results$prediction, TRUE, FALSE)

ggplot(results, aes(x = prediction, fill = correct)) +
  geom_bar(position = "dodge")
```



```
ggplot(results, aes(x = prediction, y = benign, color = correct, shape = correct)) +
  geom_jitter(size = 3, alpha = 0.6)
```



Feature Selection

Machine learning uses so called features (i.e. variables or attributes) to generate predictive models. Using a suitable combination of features is essential for obtaining high precision and accuracy. Because too many (unspecific) features pose the problem of overfitting the model, we generally want to restrict the features in our models to those, that are most relevant for the response variable we want to predict. Using as few features as possible will also reduce the complexity of our models, which means it needs less time and computer power to run and is easier to understand.

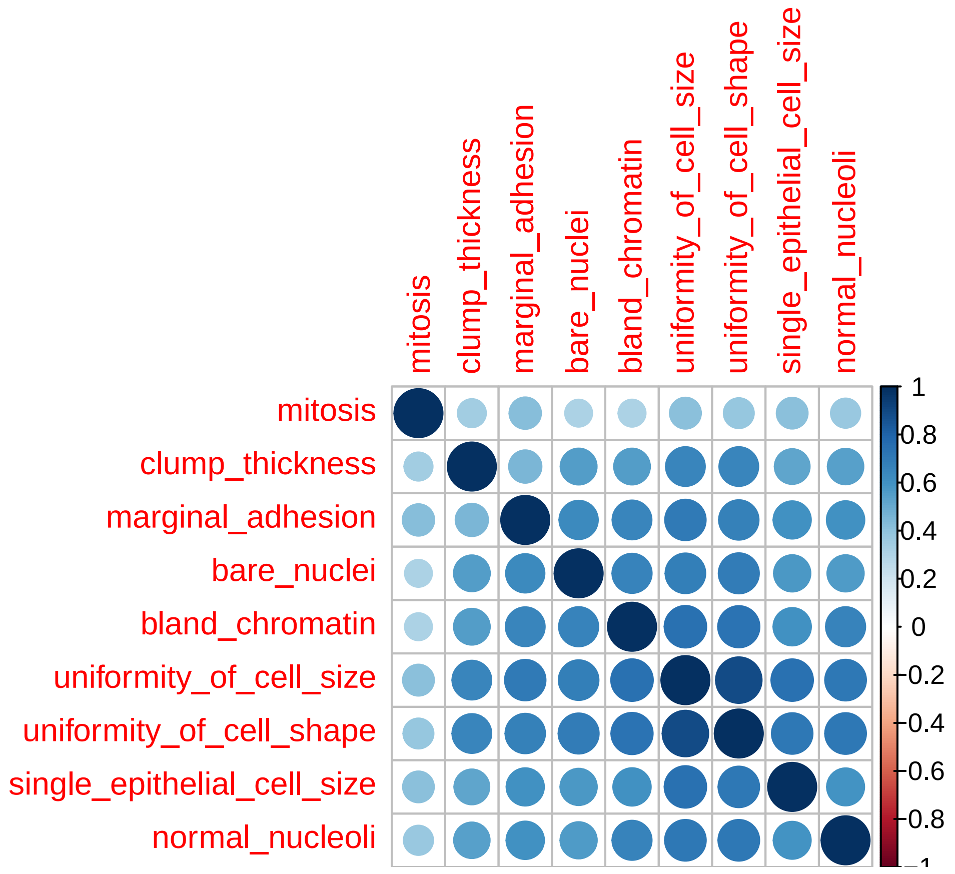
Performing feature selection on the whole dataset would lead to prediction bias, we therefore need to run the whole modeling process on the training data alone!

- Correlation

Often we have features that are highly correlated and thus provide redundant information. By eliminating highly correlated features we can avoid a predictive bias for the information contained in these features. This also shows us, that when we want to make statements about the biological/ medical importance of specific features, we need to keep in mind that just because they are suitable to predicting an outcome they are not necessarily causal - they could simply be correlated with causal factors.

Correlations between all features are calculated and visualised with the *corrplot* package. I am then removing all features with a correlation higher than 0.7, keeping the feature with the lower mean.

```
library(corrplot)

# calculate correlation matrix
corMatMy <- cor(train_data[, -1])
corrplot(corMatMy, order = "hclust")
```



```
#Apply correlation filter at 0.70,
highlyCor <- colnames(train_data[, -1])[findCorrelation(corMatMy, cutoff = 0.7, verbose = TRUE)]
```

```
## Compare row 2  and column  3 with corr  0.899
##   Means:  0.696 vs 0.575 so flagging column 2
## Compare row 3  and column  7 with corr  0.736
##   Means:  0.654 vs 0.55 so flagging column 3
## All correlations <= 0.7
```

```
# which variables are flagged for removal?
highlyCor
```

```
## [1] "uniformity_of_cell_size"  "uniformity_of_cell_shape"
```

```
#then we remove these variables
train_data_cor <- train_data[, which(!colnames(train_data) %in% highlyCor)]
```

- Recursive Feature Elimination (RFE)

Another way to choose features is with Recursive Feature Elimination. RFE uses a Random Forest algorithm to test combinations of features and rate each with an accuracy score. The combination with the highest score is usually preferential.

```
# chosen features
predictors(results_rfe)
```

```
## [1] "bare_nuclei"                 "uniformity_of_cell_size"
## [3] "clump_thickness"             "uniformity_of_cell_shape"
## [5] "bland_chromatin"             "marginal_adhesion"
## [7] "normal_nucleoli"              "single_epithelial_cell_size"
## [9] "mitosis"
```

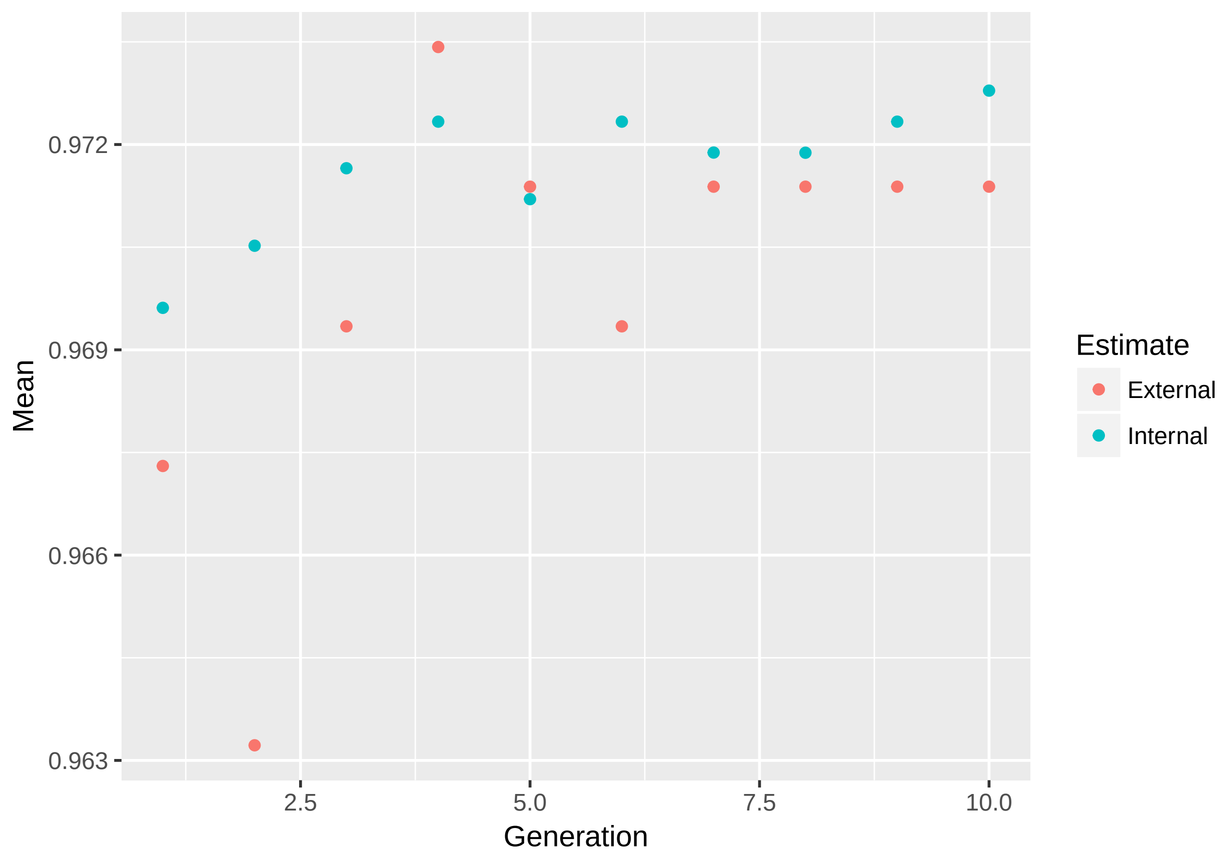
```
train_data_rfe <- train_data[, c(1, which(colnames(train_data) %in% predictors(results_rfe)))]
```

- Genetic Algorithm (GA)

The Genetic Algorithm (GA) has been developed based on evolutionary principles of natural selection: It aims to optimize a population of individuals with a given set of genotypes by modeling selection over time. In each generation (i.e. iteration), each individual's fitness is calculated based on their genotypes. Then, the fittest individuals are chosen to produce the next generation. This subsequent generation of individuals will have genotypes resulting from (re-) combinations of the parental alleles. These new genotypes will again determine each individual's fitness. This selection process is iterated for a specified number of generations and (ideally) leads to fixation of the fittest alleles in the gene pool.

This concept of optimization can be applied to non-evolutionary models as well, like feature selection processes in machine learning.

```
plot(model_ga) # Plot mean fitness (AUC) by generation
```



```
train_data_ga <- train_data[, c(1, which(colnames(train_data) %in% model_ga$ga$final))]
```

Grid search with caret

- Automatic Grid

There are two ways to tune an algorithm in the Caret R package, the first is by allowing the system to do it automatically. This can be done by setting the tuneLength to indicate the number of different values to try for each algorithm parameter.

This only supports integer and categorical algorithm parameters, and it makes a crude guess as to what values to try, but it can get you up and running very quickly.

One search strategy that we can use is to try random values within a range.

This can be good if we are unsure of what the value might be and we want to overcome any biases we may have for setting the parameter (like the suggested equation above).

Let's try a random search for mtry using caret:

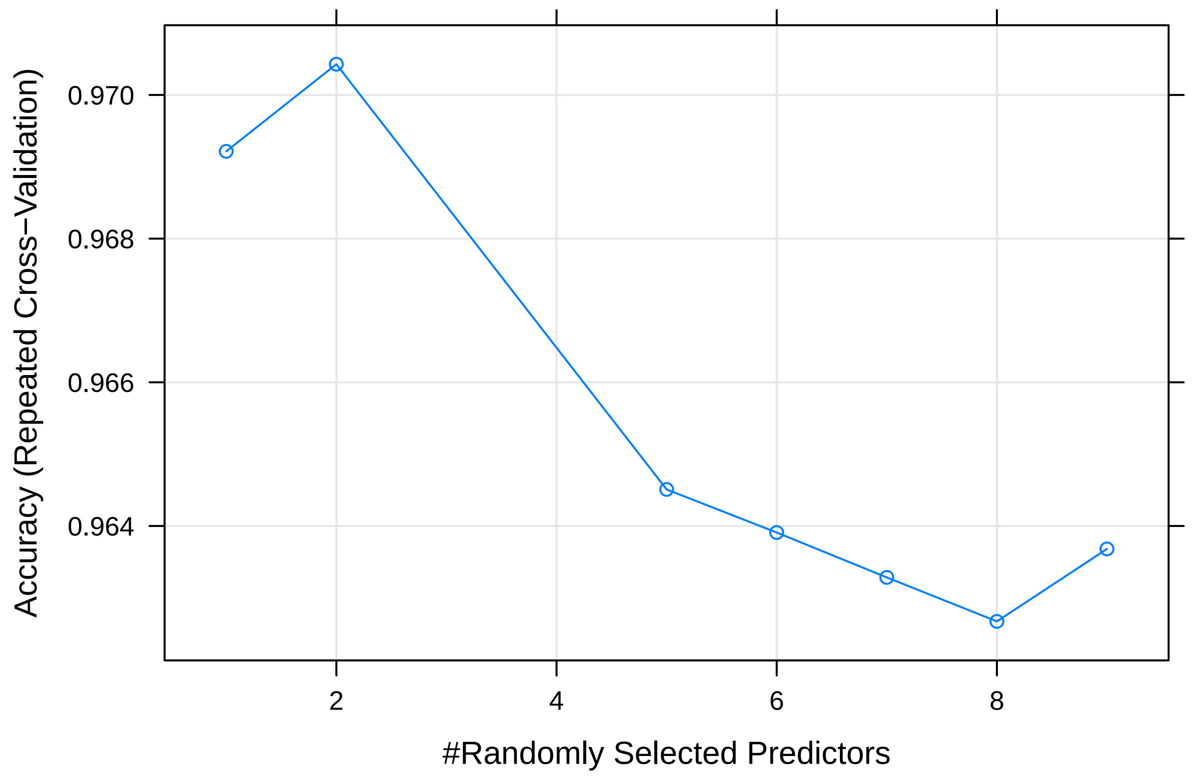
```
set.seed(42)
model_rf_tune_auto <- caret::train(classes ~ .,
                         data = train_data,
                         method = "rf",
                         preProcess = c("scale", "center"),
                         trControl = trainControl(method = "repeatedcv",
                                                  number = 10,
                                                  repeats = 10,
                                                  savePredictions = TRUE,
                                                  verboseIter = FALSE,
                                                  search = "random"),
                         tuneLength = 15)
```

When you specify `savePredictions = TRUE`, you can access the cross-validation resuls with `model_rf$pred`.

```
model_rf_tune_auto
```

```
## Random Forest
##
## 490 samples
##   9 predictor
##   2 classes: 'benign', 'malignant'
##
## Pre-processing: scaled (9), centered (9)
## Resampling: Cross-Validated (10 fold, repeated 10 times)
## Summary of sample sizes: 442, 441, 441, 441, 441, 441, ...
## Resampling results across tuning parameters:
##
##   mtry  Accuracy   Kappa
##   1     0.9692153  0.9323624
##   2     0.9704277  0.9350498
##   5     0.9645085  0.9216721
##   6     0.9639087  0.9201998
##   7     0.9632842  0.9186919
##   8     0.9626719  0.9172257
##   9     0.9636801  0.9195036
##
## Accuracy was used to select the optimal model using  the largest value.
## The final value used for the model was mtry = 2.
```

```r
plot(model_rf_tune_auto)
```



- Manual Grid

The second way to search algorithm parameters is to specify a tune grid manually. In the grid, each algorithm parameter can be specified as a vector of possible values. These vectors combine to define all the possible combinations to try.

- mtry: Number of variables randomly sampled as candidates at each split.

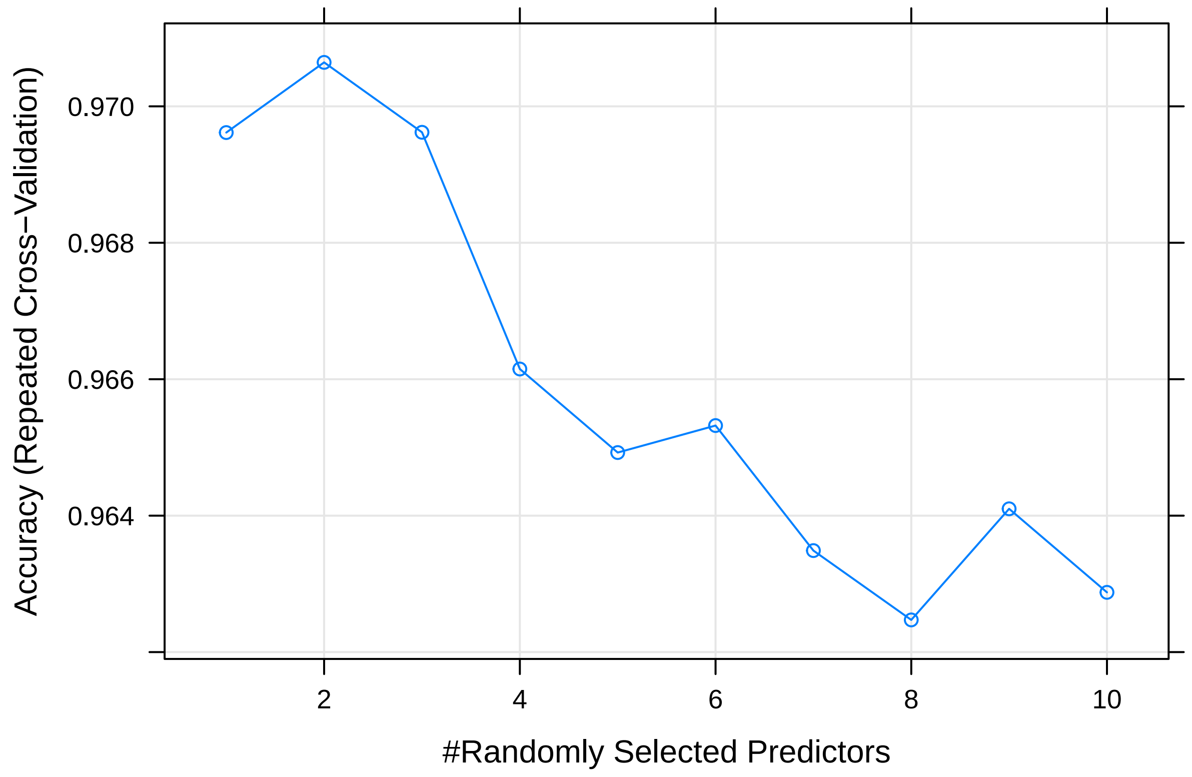
By default the only parameter you can tune for a random forest is mtry. However you can still pass the others parameters to train. But those will have a fix value an so won't be tuned by train.

```r
set.seed(42)
grid <- expand.grid(mtry = c(1:10))

model_rf_tune_man <- caret::train(classes ~ .,
                         data = train_data,
                         method = "rf",
                         preProcess = c("scale", "center"),
                         trControl = trainControl(method = "repeatedcv",
                                                  number = 10,
                                                  repeats = 10,
                                                  savePredictions = TRUE,
                                                  verboseIter = FALSE,
                                                  search = "random"),
                         tuneGrid = grid)
```

```
model_rf_tune_man
```

```
## Random Forest
##
## 490 samples
##   9 predictor
##   2 classes: 'benign', 'malignant'
##
## Pre-processing: scaled (9), centered (9)
## Resampling: Cross-Validated (10 fold, repeated 10 times)
## Summary of sample sizes: 442, 441, 441, 441, 441, 441, ...
## Resampling results across tuning parameters:
##
##   mtry  Accuracy   Kappa
##    1    0.9696153  0.9332392
##    2    0.9706440  0.9354737
##    3    0.9696194  0.9330647
##    4    0.9661495  0.9253163
##    5    0.9649252  0.9225586
##    6    0.9653209  0.9233806
##    7    0.9634881  0.9192265
##    8    0.9624718  0.9169227
##    9    0.9641005  0.9203072
##   10    0.9628760  0.9176675
##
## Accuracy was used to select the optimal model using  the largest value.
## The final value used for the model was mtry = 2.
```

```
plot(model_rf_tune_man)
```



Grid search with h2o

The R package h2o provides a convenient interface to H2O, which is an open-source machine learning and deep learning platform. H2O distributes a wide range of common machine learning algorithms for classification, regression and deep learning.

```
library(h2o)
h2o.init(nthreads = -1)
```

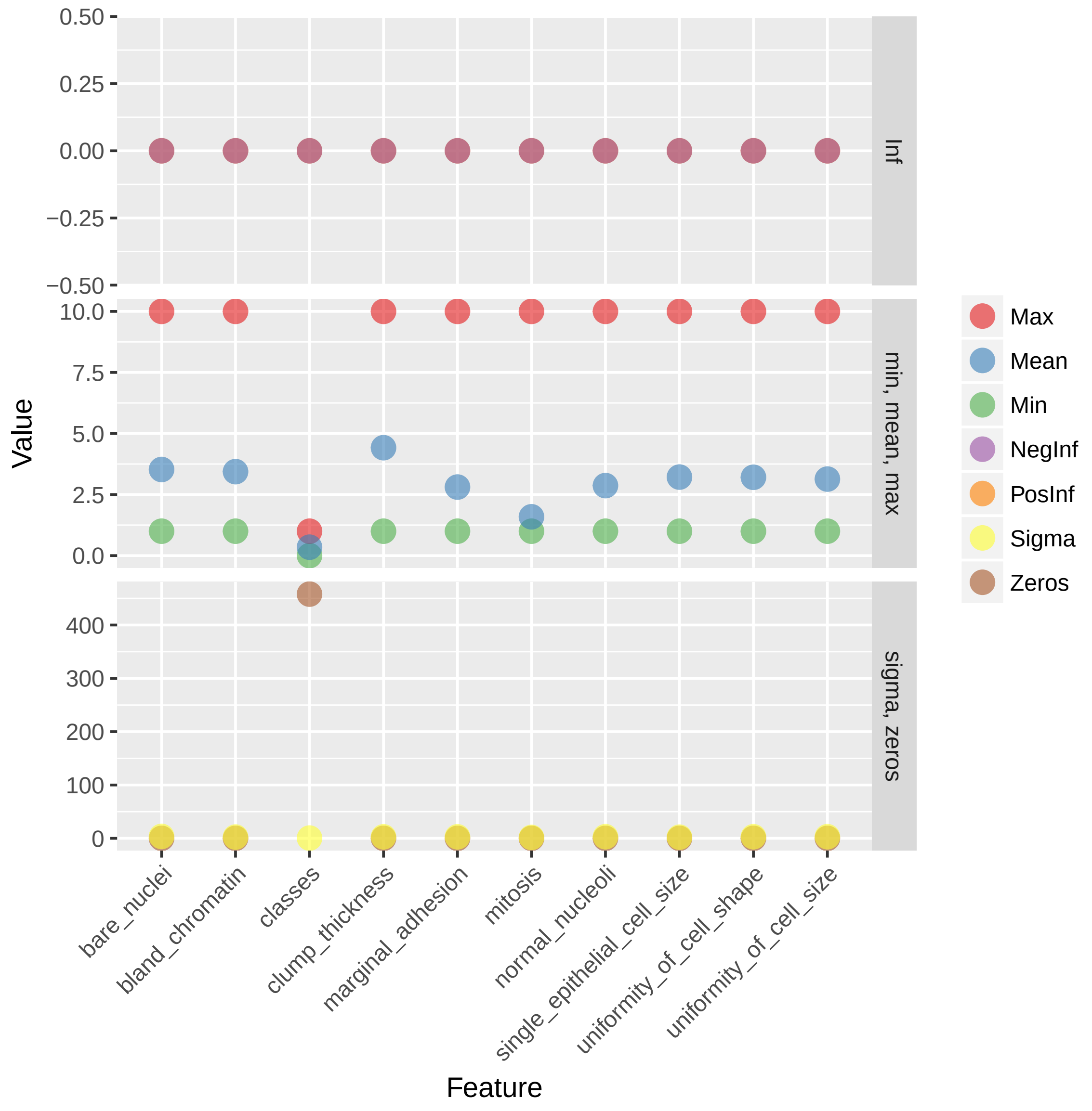
```
##  Connection successful!
##
## R is connected to the H2O cluster:
##     H2O cluster uptime:         37 minutes 47 seconds
##     H2O cluster version:        3.10.3.6
##     H2O cluster version age:    1 month and 6 days
##     H2O cluster name:           H2O_started_from_R_s_glan02_ogq244
##     H2O cluster total nodes:    1
##     H2O cluster total memory:   3.30 GB
##     H2O cluster total cores:    8
##     H2O cluster allowed cores:  8
##     H2O cluster healthy:        TRUE
##     H2O Connection ip:          localhost
##     H2O Connection port:        54321
##     H2O Connection proxy:       NA
##     R Version:                  R version 3.3.3 (2017-03-06)
```

```r
bc_data_hf <- as.h2o(bc_data)
```

```
##
  |
  |                                                                 |   0%
  |
  |=================================================================| 100%
```

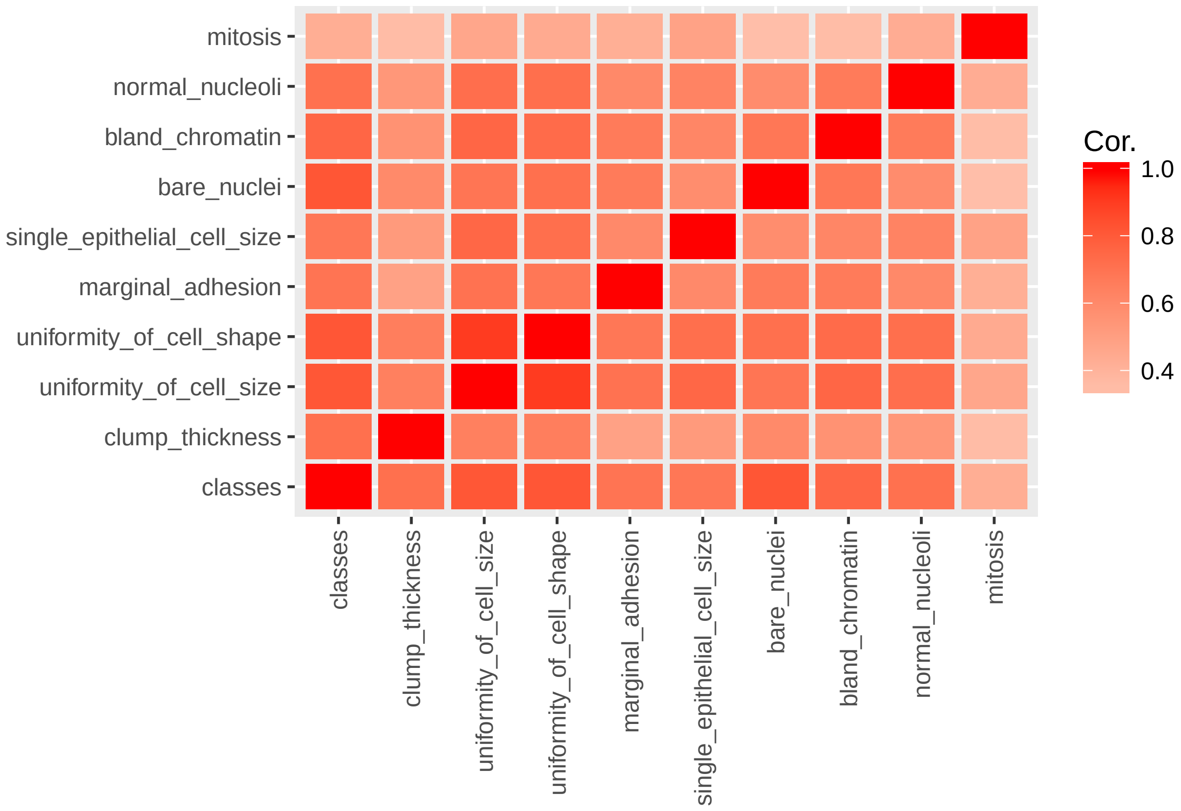
We can now access all functions from the **h2o** package that are built to work on H2O Frames. A useful such function is *h2o.describe()*. It is similar to base R's *summary()* function but outputs many more descriptive measures for our data. To get a good overview about these measures, I am going to plot them.

```r
h2o.describe(bc_data_hf) %>%
  gather(x, y, Zeros:Sigma) %>%
  mutate(group = ifelse(x %in% c("Min", "Max", "Mean"), "min, mean, max",
                        ifelse(x %in% c("NegInf", "PosInf"), "Inf", "sigma, zeros"))) %>%
  ggplot(aes(x = Label, y = as.numeric(y), color = x)) +
    geom_point(size = 4, alpha = 0.6) +
    scale_color_brewer(palette = "Set1") +
    theme(axis.text.x = element_text(angle = 45, vjust = 1, hjust = 1)) +
    facet_grid(group ~ ., scales = "free") +
    labs(x = "Feature",
         y = "Value",
         color = "")
```



I am also interested in the correlation between features and the output. We can use the *h2o.cor()* function to calculate the correlation matrix. It is again much easier to understand the data when we visualize it, so I am going to create another plot.

```
library(reshape2) # for melting

bc_data_hf[, 1] <- h2o.asfactor(bc_data_hf[, 1])

cor <- h2o.cor(bc_data_hf)
rownames(cor) <- colnames(cor)

melt(cor) %>%
  mutate(Var2 = rep(rownames(cor), nrow(cor))) %>%
  mutate(Var2 = factor(Var2, levels = colnames(cor))) %>%
  mutate(variable = factor(variable, levels = colnames(cor))) %>%
  ggplot(aes(x = variable, y = Var2, fill = value)) +
    geom_tile(width = 0.9, height = 0.9) +
    scale_fill_gradient2(low = "white", high = "red", name = "Cor.") +
    theme(axis.text.x = element_text(angle = 90, vjust = 0.5, hjust = 1)) +
    labs(x = "",
         y = "")
```



Training, validation and test data

Now we can use the *h2o.splitFrame()* function to split the data into training, validation and test data. Here, I am using 70% for training and 15% each for validation and testing. We could also just split the data into two sections, a training and test set but when we have sufficient samples, it is a good idea to evaluate model performance on an independent test set on top of training with a validation set. Because we can easily overfit a model, we want to get an idea about how generalizable it is - this we can only assess by looking at how well it works on previously unknown data.

I am also defining response and feature column names now.

```
splits <- h2o.splitFrame(bc_data_hf,
                         ratios = c(0.7, 0.15),
                         seed = 1)

train <- splits[[1]]
valid <- splits[[2]]
test <- splits[[3]]

response <- "classes"
features <- setdiff(colnames(train), response)
```

```r
summary(train$classes, exact_quantiles = TRUE)
```

```
##  classes
##  benign   :317
##  malignant:174
```

```r
summary(valid$classes, exact_quantiles = TRUE)
```

```
##  classes
##  benign   :71
##  malignant:35
```

```r
summary(test$classes, exact_quantiles = TRUE)
```

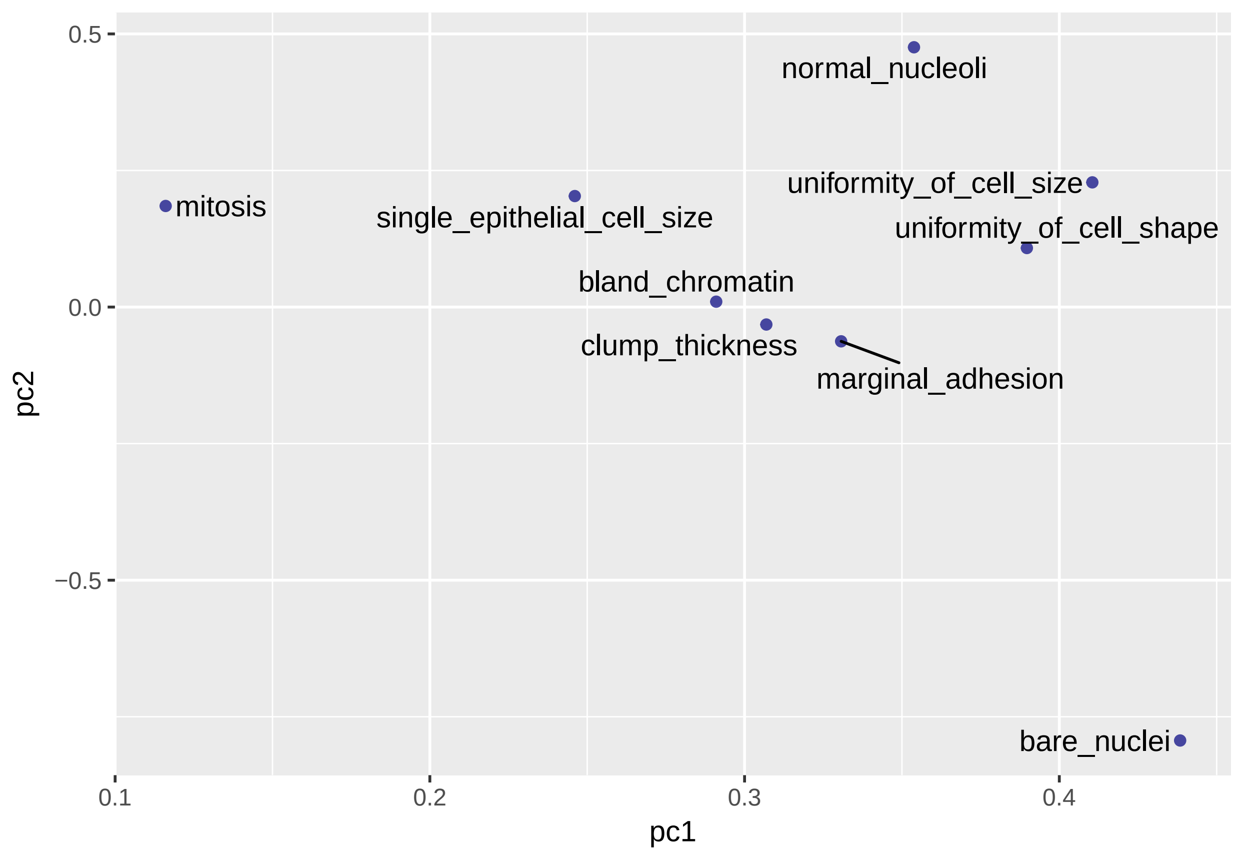
```
##  classes
##  benign   :70
##  malignant:32
```

We can also run a PCA on the training data, using the *h2o.prcomp()* function to calculate the singular value decomposition of the Gram matrix with the power method.

```r
pca <- h2o.prcomp(training_frame = train,
           x = features,
           validation_frame = valid,
           transform = "NORMALIZE",
           impute_missing = TRUE,
           k = 3,
           seed = 42)
```

```
##
  |
  |                                                                 |   0%
  |
  |=================================================================| 100%
```

```r
eigenvec <- as.data.frame(pca@model$eigenvectors)
eigenvec$label <- features

library(ggrepel)
ggplot(eigenvec, aes(x = pc1, y = pc2, label = label)) +
  geom_point(color = "navy", alpha = 0.7) +
  geom_text_repel()
```



Classification

We can use the `h2o.grid()` function to perform a Random Grid Search (RGS). We could also test all possible combinations of parameters with Cartesian Grid or exhaustive search, but RGS is much faster when we have a large number of possible combinations and usually finds sufficiently accurate models.

For RGS, we first define a set of hyper-parameters and search criteria to fine-tune our models. Because there are many hyper-parameters, each with a range of possible values, we want to find an (ideally) optimal combination to maximize our model's accuracy. We can also specify how long we want to run the grid search for. Based on the results of each model tested in the grid, we can choose the one with the highest accuracy or best performance for the question on hand.

Random Forest

```
hyper_params <- list(
                     ntrees = c(25, 50, 75, 100),
                     max_depth = c(10, 20, 30),
                     min_rows = c(1, 3, 5)
                     )

search_criteria <- list(
                        strategy = "RandomDiscrete",
                        max_models = 50,
                        max_runtime_secs = 360,
                        stopping_rounds = 5,
                        stopping_metric = "AUC",
```

```r
                        stopping_tolerance = 0.0005,
                        seed = 42
                        )
```

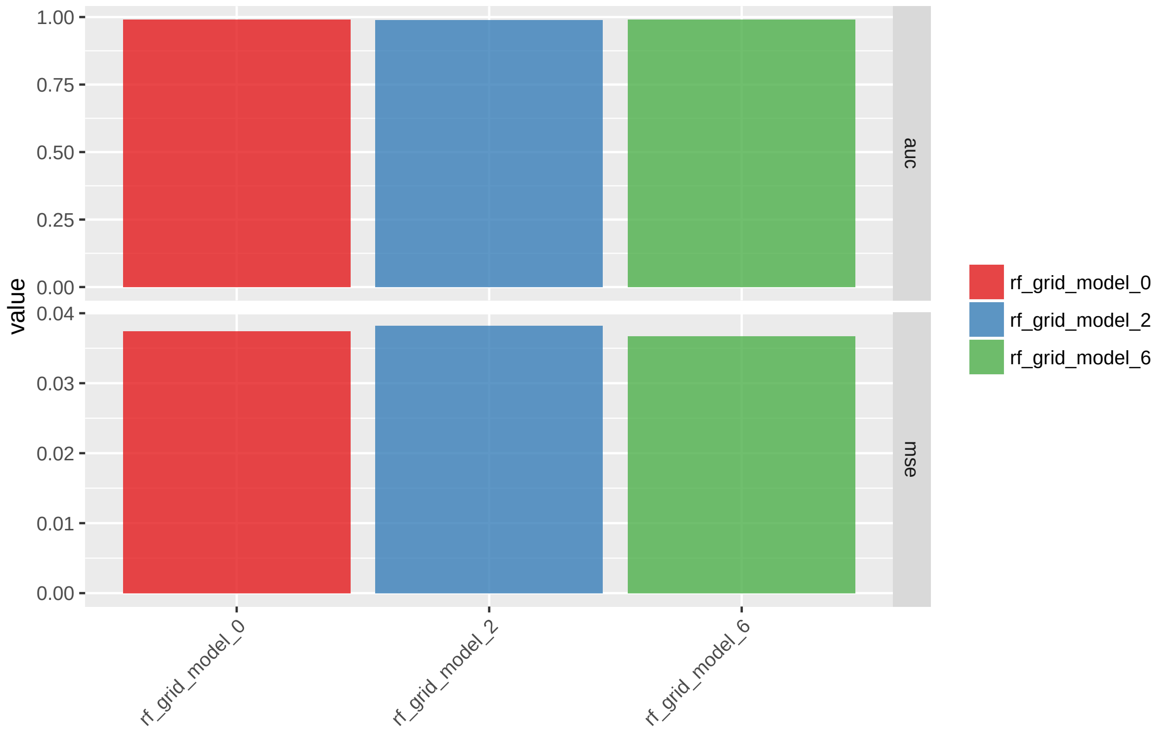
```r
rf_grid <- h2o.grid(algorithm = "randomForest", # h2o.randomForest,
                                                # alternatively h2o.gbm for Gradient boosting trees
                    x = features,
                    y = response,
                    grid_id = "rf_grid",
                    training_frame = train,
                    validation_frame = valid,
                    nfolds = 25,
                    fold_assignment = "Stratified",
                    hyper_params = hyper_params,
                    search_criteria = search_criteria,
                    seed = 42
                    )
```

We now want to extract the best model from the grid model list. What makes a model *the best* depends on the question you want to address with it: in some cases, the model with highest AUC is the most suitable, or the one with the lowest mean squared error, etc. We first use the `h2o.getGrid()` function to sort all models by the quality metric we choose (depending on the metric, you want it ordered by descending or ascending values). We can then get the model that's the first in the list to work with further. This model's hyper-parameters can be found with `best_model@allparameters`. You can now work with your best model as with any regular model in **h2o**.

```r
# performance metrics where smaller is better -> order with decreasing = FALSE
sort_options_1 <- c("mean_per_class_error", "mse", "err", "logloss")

for (sort_by_1 in sort_options_1) {

  grid <- h2o.getGrid("rf_grid", sort_by = sort_by_1, decreasing = FALSE)

  model_ids <- grid@model_ids
  best_model <- h2o.getModel(model_ids[[1]])

  h2o.saveModel(best_model, path="models", force = TRUE)

}


# performance metrics where bigger is better -> order with decreasing = TRUE
sort_options_2 <- c("auc", "precision", "accuracy", "recall", "specificity")

for (sort_by_2 in sort_options_2) {

  grid <- h2o.getGrid("rf_grid", sort_by = sort_by_2, decreasing = TRUE)

  model_ids <- grid@model_ids
  best_model <- h2o.getModel(model_ids[[1]])

  h2o.saveModel(best_model, path = "models", force = TRUE)

}
```

The ultimate performance test for our model will be it's prediction accuracy on the test set it hasn't seen before. Here, I will compare the AUC and mean squared error for each best model from before. You could of course look at any other quality metric that is most appropriate for your model.

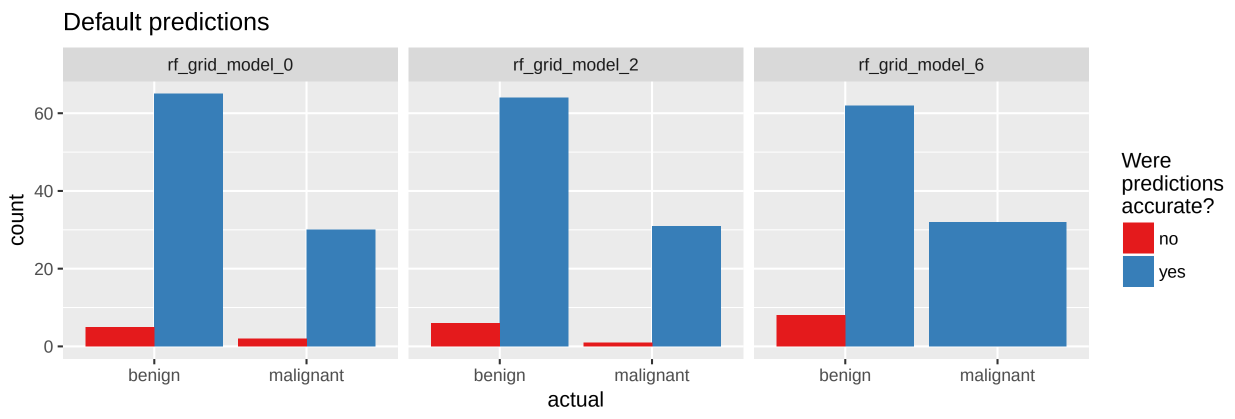
```r
files <- list.files(path = "models")
rf_models <- files[grep("rf_grid_model", files)]

for (model_id in rf_models) {

  path <- paste0("U:\\Github_blog\\Webinar\\Webinar_ML_for_disease\\models\\", model_id)
  #path <- paste0("/Users/Shirin/Documents/Github/Webinar_ML_for_disease/models/", model_id)
  best_model <- h2o.loadModel(path)
  mse_auc_test <- data.frame(model_id = model_id,
                             mse = h2o.mse(h2o.performance(best_model, test)),
                             auc = h2o.auc(h2o.performance(best_model, test)))

  if (model_id == rf_models[[1]]) {

    mse_auc_test_comb <- mse_auc_test

  } else {

    mse_auc_test_comb <- rbind(mse_auc_test_comb, mse_auc_test)

  }
}

mse_auc_test_comb %>%
  gather(x, y, mse:auc) %>%
  ggplot(aes(x = model_id, y = y, fill = model_id)) +
    facet_grid(x ~ ., scales = "free") +
    geom_bar(stat = "identity", alpha = 0.8, position = "dodge") +
    scale_fill_brewer(palette = "Set1") +
    theme(axis.text.x = element_text(angle = 45, vjust = 1, hjust = 1),
          plot.margin = unit(c(0.5, 0, 0, 1.5), "cm")) +
    labs(x = "", y = "value", fill = "")
```



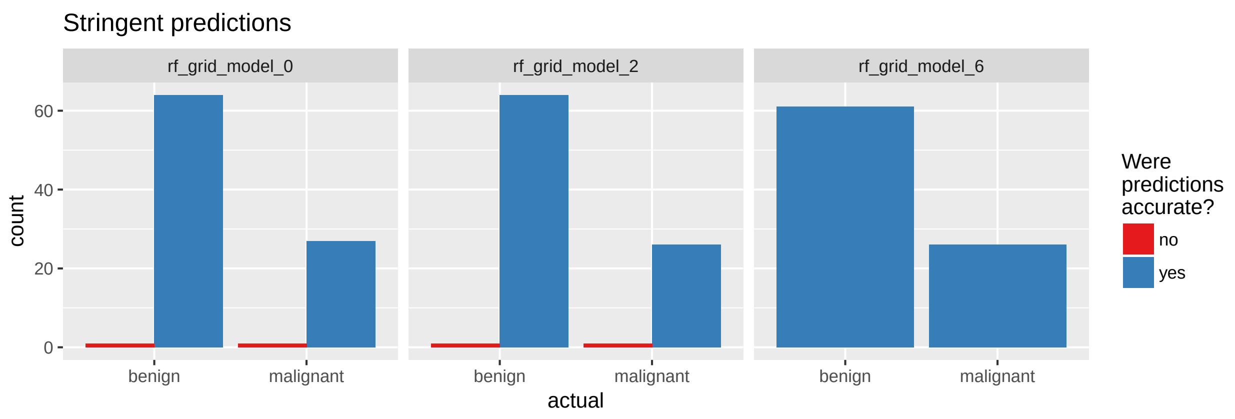
```
for (model_id in rf_models) {

  best_model <- h2o.getModel(model_id)

  finalRf_predictions <- data.frame(model_id = rep(best_model@model_id,
                                                    nrow(test)),
                                    actual = as.vector(test$classes),
                                    as.data.frame(h2o.predict(object = best_model,
                                                              newdata = test)))

  finalRf_predictions$accurate <- ifelse(finalRf_predictions$actual == finalRf_predictions$predict,
                                         "yes", "no")

  finalRf_predictions$predict_stringent <- ifelse(finalRf_predictions$benign > 0.8,
                                                  "benign",
                                                  ifelse(finalRf_predictions$malignant > 0.8,
                                                         "malignant", "uncertain"))

  finalRf_predictions$accurate_stringent <- ifelse(finalRf_predictions$actual == finalRf_predictions$pre
                                                   "yes",
                                         ifelse(finalRf_predictions$predict_stringent == "uncertain",
                                                "na", "no"))

  if (model_id == rf_models[[1]]) {

    finalRf_predictions_comb <- finalRf_predictions

  } else {
    finalRf_predictions_comb <- rbind(finalRf_predictions_comb, finalRf_predictions)

  }
}
```

```
##
  |
  |                                                                 |   0%
  |
  |=================================================================| 100%
##
  |
  |                                                                 |   0%
  |
  |=================================================================| 100%
##
  |
  |                                                                 |   0%
  |
  |=================================================================| 100%
```

```
finalRf_predictions_comb %>%
  ggplot(aes(x = actual, fill = accurate)) +
    geom_bar(position = "dodge") +
    scale_fill_brewer(palette = "Set1") +
    facet_wrap(~ model_id, ncol = 3) +
    labs(fill = "Were\npredictions\naccurate?",
         title = "Default predictions")
```

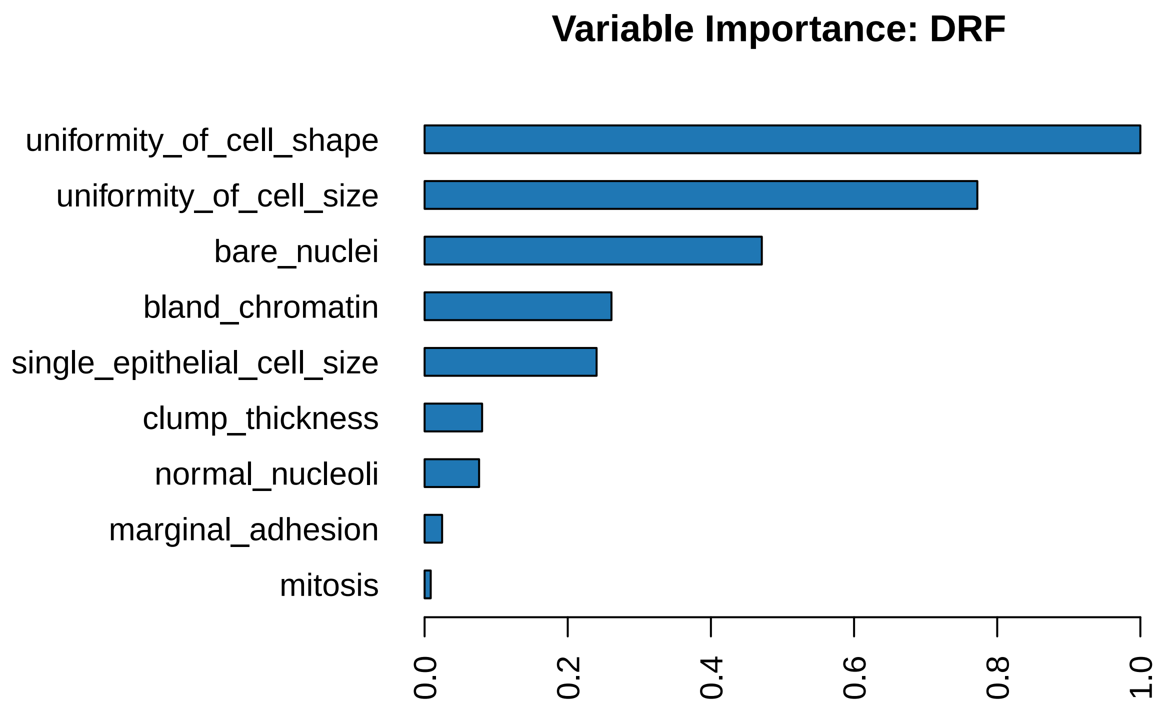


```
finalRf_predictions_comb %>%
  subset(accurate_stringent != "na") %>%
  ggplot(aes(x = actual, fill = accurate_stringent)) +
    geom_bar(position = "dodge") +
    scale_fill_brewer(palette = "Set1") +
    facet_wrap(~ model_id, ncol = 3) +
    labs(fill = "Were\npredictions\naccurate?",
         title = "Stringent predictions")
```



```r
rf_model <- h2o.loadModel("U:\\Github_blog\\Webinar\\Webinar_ML_for_disease\\models\\rf_grid_model_6")
#rf_model <- h2o.loadModel("models/rf_grid_model_6")
#summary(rf_model)
#str(rf_model)
```

```r
h2o.varimp_plot(rf_model)
```



```r
#h2o.varimp(rf_model)
```

One performance metric we are interested in is the mean per class error for training and validation data.

```r
h2o.mean_per_class_error(rf_model, train = TRUE, valid = TRUE, xval = TRUE)
```

```
##       train       valid        xval
## 0.024674571 0.007042254 0.023097284
```

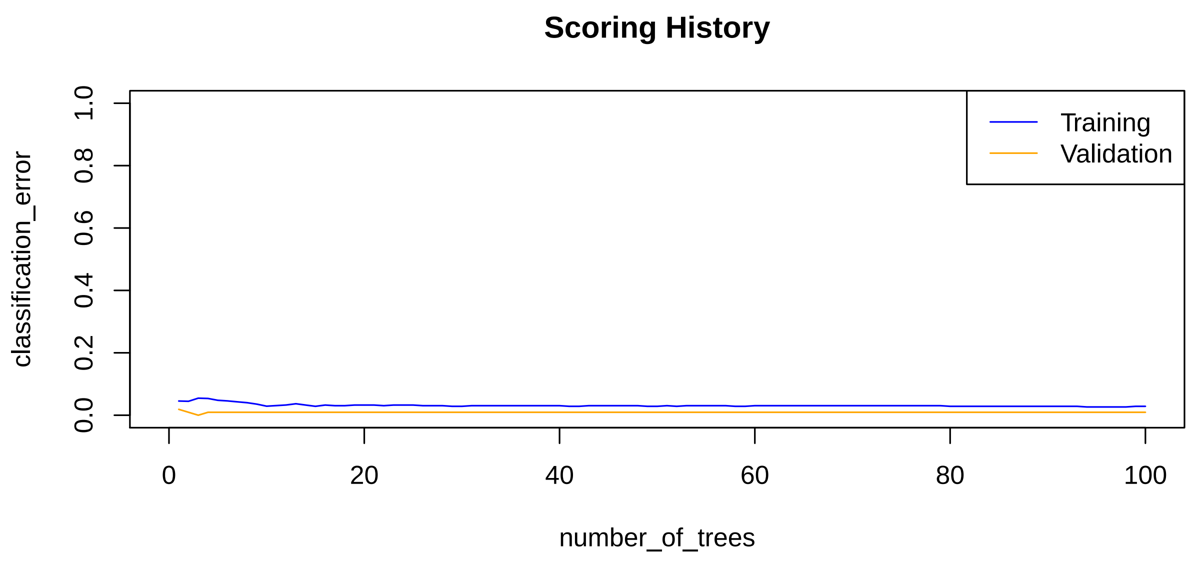
The confusion matrix tells us, how many classes have been predicted correctly and how many predictions were accurate. Here, we see the errors in predictions on validation data

```
h2o.confusionMatrix(rf_model, valid = TRUE)
```

```
## Confusion Matrix (vertical: actual; across: predicted)  for max f1 @ threshold = 0.293125896751881:
##           benign malignant    Error     Rate
## benign        70         1 0.014085    =1/71
## malignant      0        35 0.000000    =0/35
## Totals        70        36 0.009434  =1/106
```

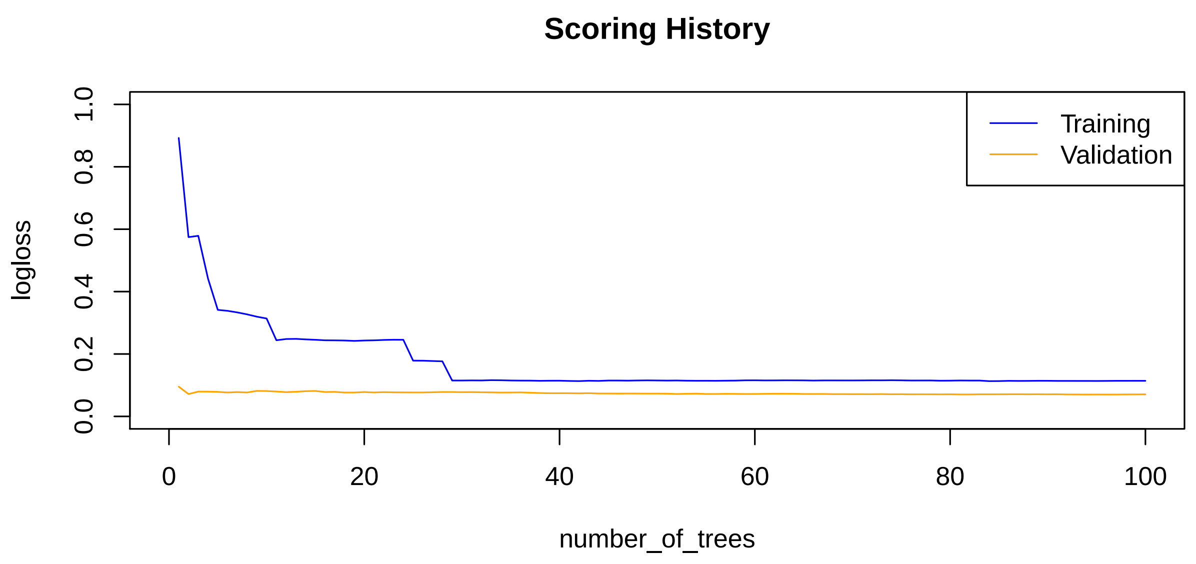
We can also plot the classification error.

```
plot(rf_model,
     timestep = "number_of_trees",
     metric = "classification_error")
```

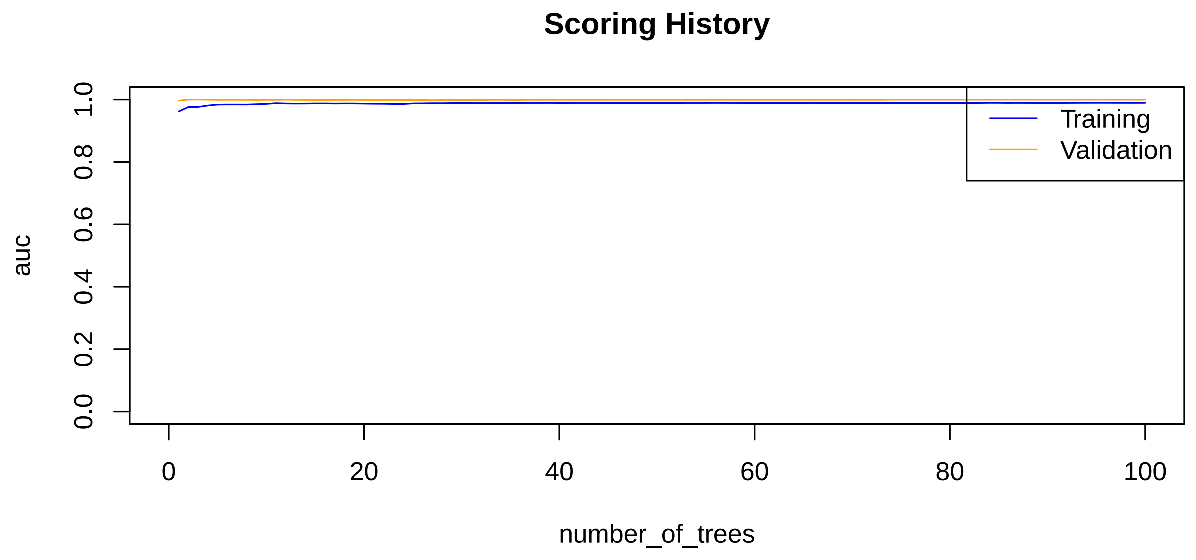


Next to the classification error, we are usually interested in the logistic loss (negative log-likelihood or log loss). It describes the sum of errors for each sample in the training or validation data or the negative logarithm of the likelihood of error for a given prediction/ classification. Simply put, the lower the loss, the better the model (if we ignore potential overfitting).

```
plot(rf_model,
     timestep = "number_of_trees",
     metric = "logloss")
```

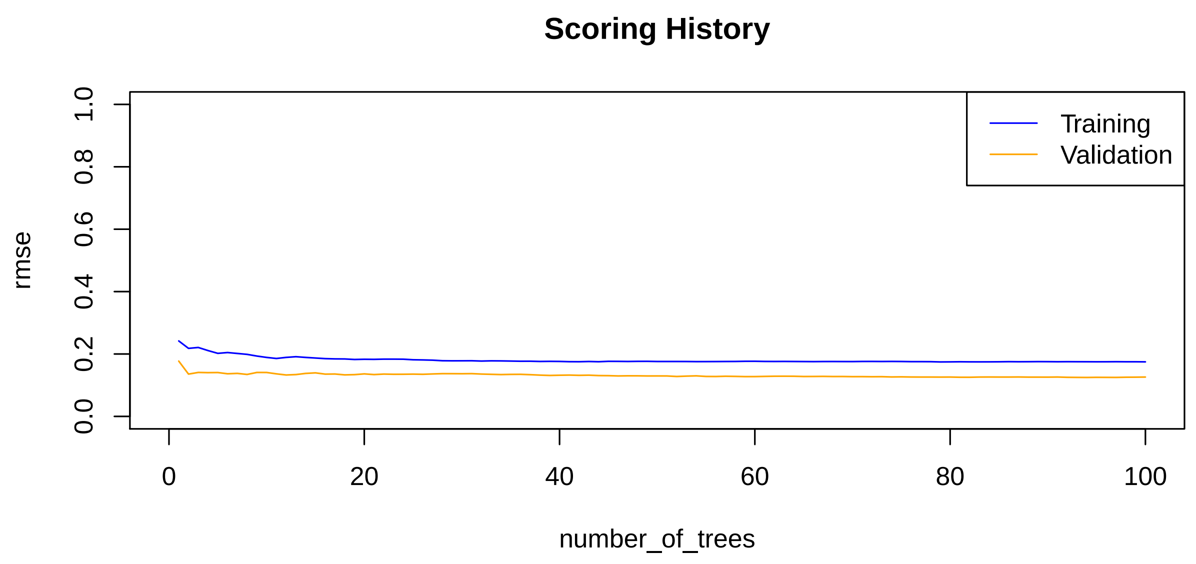


```r
plot(rf_model,
     timestep = "number_of_trees",
     metric = "AUC")
```



We can also plot the mean squared error (MSE). The MSE tells us the average of the prediction errors squared, i.e. the estimator's variance and bias. The closer to zero, the better a model.

```r
plot(rf_model,
     timestep = "number_of_trees",
     metric = "rmse")
```



Next, we want to know the area under the curve (AUC). AUC is an important metric for measuring binary classification model performances. It gives the area under the curve, i.e. the integral, of true positive vs false positive rates. The closer to 1, the better a model. AUC is especially useful, when we have unbalanced datasets (meaning datasets where one class is much more common than the other), because it is independent of class labels.

```
h2o.auc(rf_model, train = TRUE)
```

```
## [1] 0.989521
```

```
h2o.auc(rf_model, valid = TRUE)
```

```
## [1] 0.9995976
```

```
h2o.auc(rf_model, xval = TRUE)
```

```
## [1] 0.9890496
```

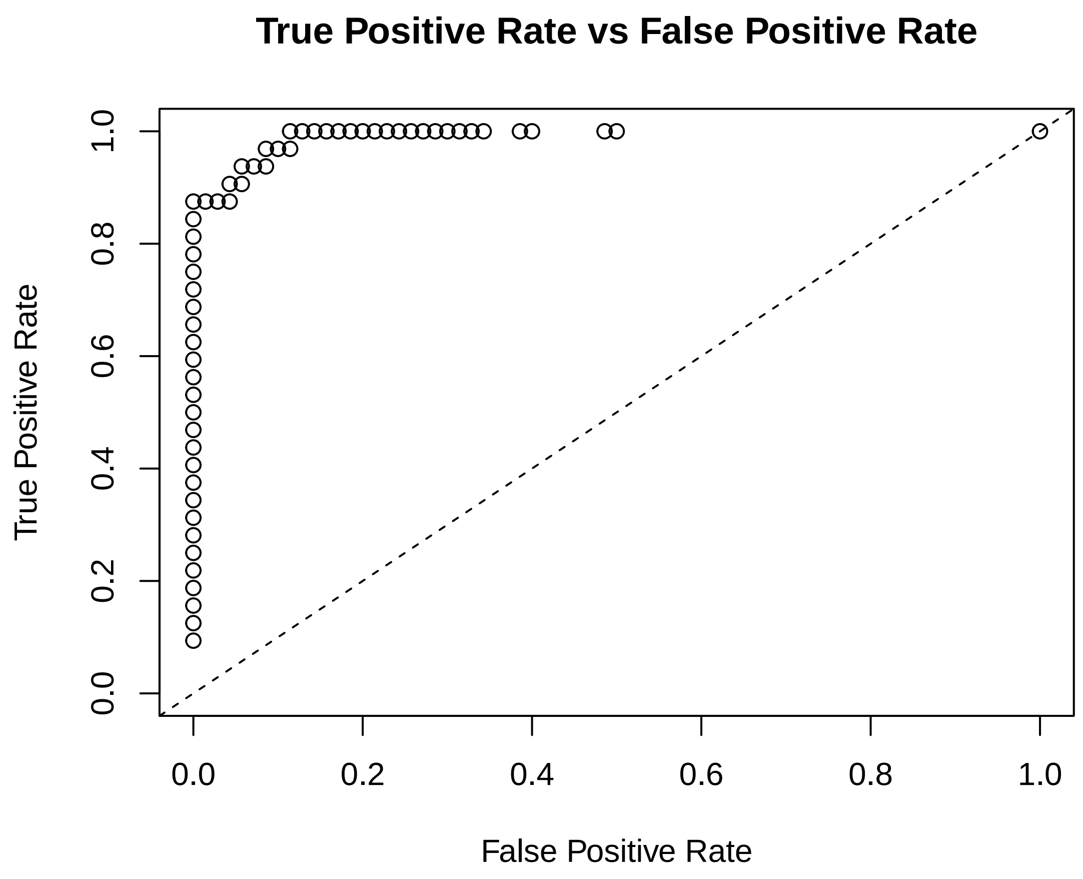
A good model should find an optimal balance between accuracy on training and test data. A model that has 0% error on the training data but 40% error on the test data is in effect useless. It overfit on the training data and is thus not able to generalize to unknown data.

```
perf <- h2o.performance(rf_model, test)
perf
```

```
## H2OBinomialMetrics: drf
##
## MSE:  0.03673598
## RMSE:  0.1916663
## LogLoss:  0.1158835
## Mean Per-Class Error:  0.0625
## AUC:  0.990625
## Gini:  0.98125
##
## Confusion Matrix (vertical: actual; across: predicted) for F1-optimal threshold:
##           benign malignant    Error    Rate
## benign        70         0 0.000000   =0/70
## malignant      4        28 0.125000   =4/32
## Totals        74        28 0.039216  =4/102
##
## Maximum Metrics: Maximum metrics at their respective thresholds
##                         metric threshold    value idx
## 1                       max f1  0.735027 0.933333  25
## 2                       max f2  0.294222 0.952381  37
## 3                 max f0point5  0.735027 0.972222  25
## 4                 max accuracy  0.735027 0.960784  25
## 5                max precision  1.000000 1.000000   0
## 6                   max recall  0.294222 1.000000  37
## 7              max specificity  1.000000 1.000000   0
## 8             max absolute_mcc  0.735027 0.909782  25
## 9   max min_per_class_accuracy  0.424524 0.937500  31
## 10 max mean_per_class_accuracy  0.294222 0.942857  37
##
## Gains/Lift Table: Extract with `h2o.gainsLift(<model>, <data>)` or `h2o.gainsLift(<model>, valid=<T/
```

Plotting the test performance's AUC plot shows us approximately how good the predictions are.

```r
plot(perf)
```



We also want to know the log loss, MSE and AUC values, as well as other model metrics for the test data:

```
h2o.logloss(perf)
```

```
## [1] 0.1158835
```

```
h2o.mse(perf)
```

```
## [1] 0.03673598
```

```
h2o.auc(perf)
```

```
## [1] 0.990625
```

```
head(h2o.metric(perf))
```

```
## Metrics for Thresholds: Binomial metrics as a function of classification thresholds
##   threshold       f1       f2 f0point5 accuracy precision   recall
## 1  1.000000 0.171429 0.114504 0.340909 0.715686  1.000000 0.093750
## 2  0.998333 0.222222 0.151515 0.416667 0.725490  1.000000 0.125000
## 3  0.998000 0.270270 0.187970 0.480769 0.735294  1.000000 0.156250
## 4  0.997222 0.315789 0.223881 0.535714 0.745098  1.000000 0.187500
## 5  0.996210 0.358974 0.259259 0.583333 0.754902  1.000000 0.218750
## 6  0.994048 0.400000 0.294118 0.625000 0.764706  1.000000 0.250000
##   specificity absolute_mcc min_per_class_accuracy mean_per_class_accuracy
## 1    1.000000     0.257464               0.093750                0.546875
## 2    1.000000     0.298807               0.125000                0.562500
## 3    1.000000     0.335794               0.156250                0.578125
## 4    1.000000     0.369755               0.187500                0.593750
## 5    1.000000     0.401478               0.218750                0.609375
## 6    1.000000     0.431474               0.250000                0.625000
##   tns fns fps tps      tnr      fnr      fpr      tpr idx
## 1  70  29   0   3 1.000000 0.906250 0.000000 0.093750   0
## 2  70  28   0   4 1.000000 0.875000 0.000000 0.125000   1
## 3  70  27   0   5 1.000000 0.843750 0.000000 0.156250   2
## 4  70  26   0   6 1.000000 0.812500 0.000000 0.187500   3
## 5  70  25   0   7 1.000000 0.781250 0.000000 0.218750   4
## 6  70  24   0   8 1.000000 0.750000 0.000000 0.250000   5
```

The final predictions with probabilities can be extracted with the *h2o.predict()* function. Beware though, that the number of correct and wrong classifications can be slightly different from the confusion matrix above. Here, I combine the predictions with the actual test diagnoses and classes into a data frame. For plotting I also want to have a column, that tells me whether the predictions were correct. By default, a prediction probability above 0.5 will get scored as a prediction for the respective category. I find it often makes sense to be more stringent with this, though and set a higher threshold. Therefore, I am creating another column with stringent predictions, where I only count predictions that were made with more than 80% probability. Everything that does not fall within this range gets scored as "uncertain". For these stringent predictions, I am also creating a column that tells me whether they were accurate.

```
finalRf_predictions <- data.frame(actual = as.vector(test$classes),
                                  as.data.frame(h2o.predict(object = rf_model, newdata = test)))
```

```
##
  |
  |                                                                 |   0%
  |
  |=================================================================| 100%
```

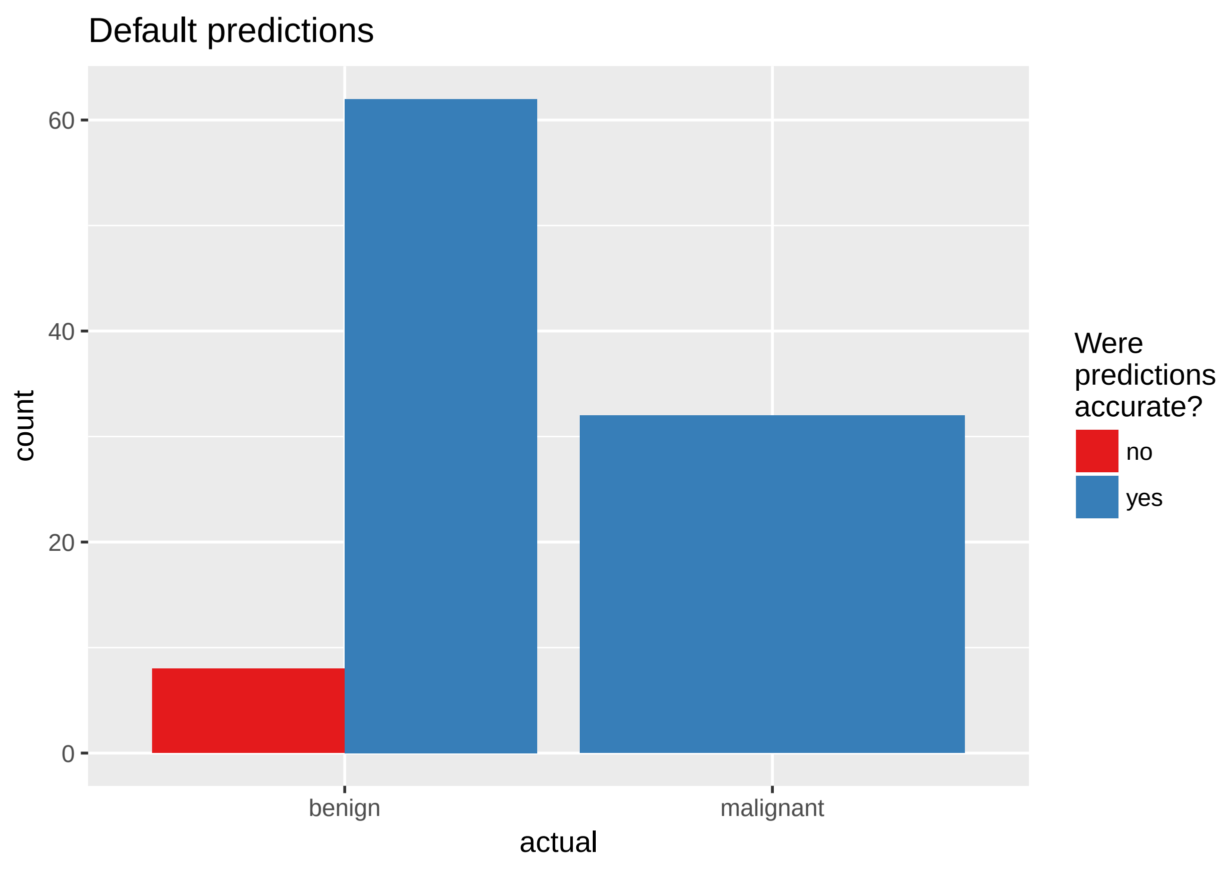
```
finalRf_predictions$accurate <- ifelse(finalRf_predictions$actual == finalRf_predictions$predict, "yes"

finalRf_predictions$predict_stringent <- ifelse(finalRf_predictions$benign > 0.8, "benign",
                                                ifelse(finalRf_predictions$malignant > 0.8, "malignant"
finalRf_predictions$accurate_stringent <- ifelse(finalRf_predictions$actual == finalRf_predictions$predi
                                       ifelse(finalRf_predictions$predict_stringent == "uncertain", "na

finalRf_predictions %>%
  group_by(actual, predict) %>%
  dplyr::summarise(n = n())
```

```
## Source: local data frame [3 x 3]
## Groups: actual [?]
##
##      actual   predict     n
##      <fctr>    <fctr> <int>
## 1    benign    benign    62
## 2    benign malignant     8
## 3 malignant malignant    32
```

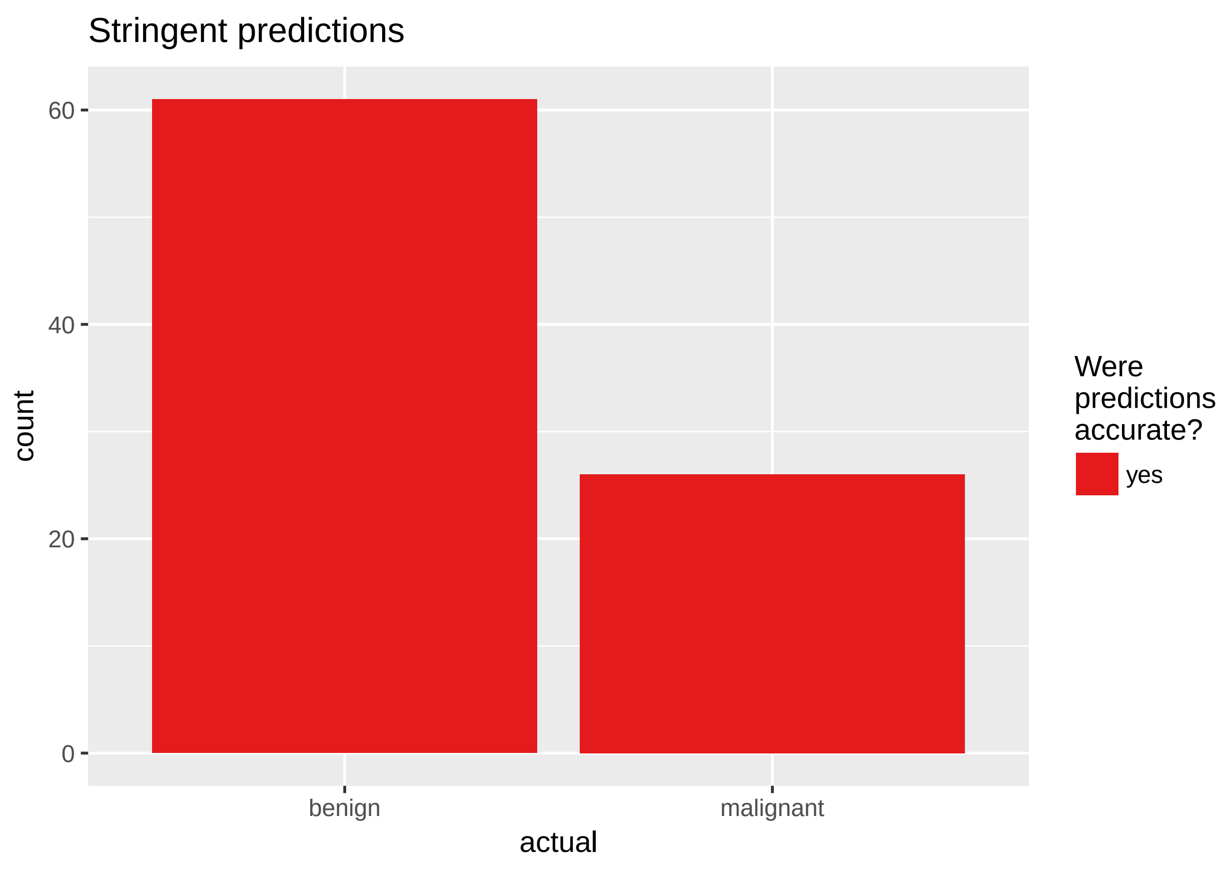
```
finalRf_predictions %>%
  group_by(actual, predict_stringent) %>%
  dplyr::summarise(n = n())
```

```
## Source: local data frame [4 x 3]
## Groups: actual [?]
##
##      actual predict_stringent     n
##      <fctr>             <chr> <int>
## 1    benign            benign    61
## 2    benign         uncertain     9
## 3 malignant         malignant    26
## 4 malignant         uncertain     6
```

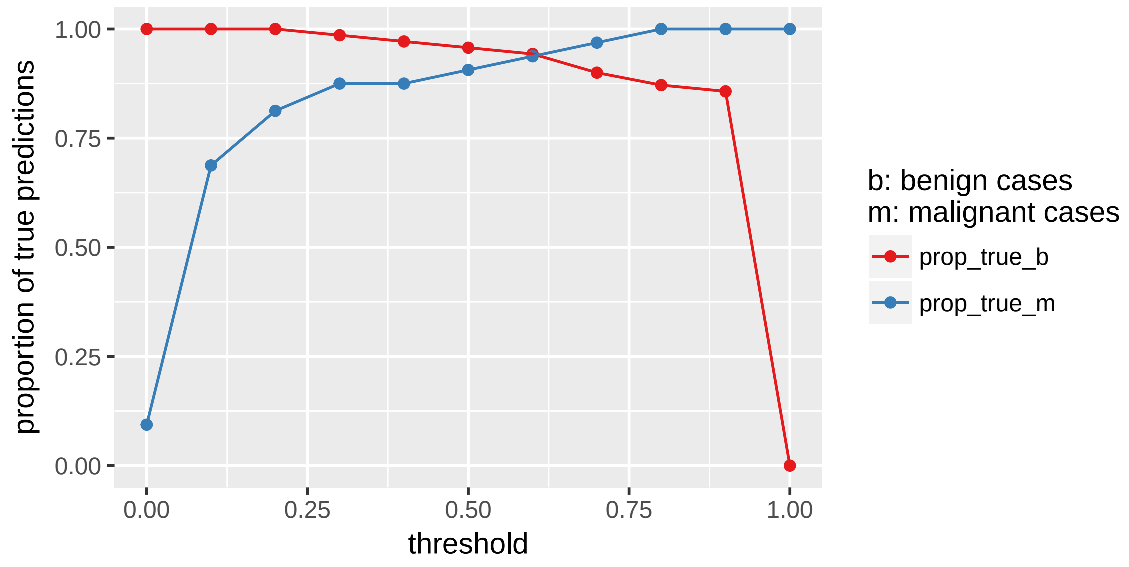
```
finalRf_predictions %>%
  ggplot(aes(x = actual, fill = accurate)) +
    geom_bar(position = "dodge") +
    scale_fill_brewer(palette = "Set1") +
    labs(fill = "Were\npredictions\naccurate?",
         title = "Default predictions")
```



```
finalRf_predictions %>%
  subset(accurate_stringent != "na") %>%
  ggplot(aes(x = actual, fill = accurate_stringent)) +
    geom_bar(position = "dodge") +
    scale_fill_brewer(palette = "Set1") +
    labs(fill = "Were\npredictions\naccurate?",
         title = "Stringent predictions")
```



```r
df <- finalRf_predictions[, c(1, 3, 4)]

thresholds <- seq(from = 0, to = 1, by = 0.1)

prop_table <- data.frame(threshold = thresholds, prop_true_b = NA, prop_true_m = NA)

for (threshold in thresholds) {
  pred <- ifelse(df$benign > threshold, "benign", "malignant")
  pred_t <- ifelse(pred == df$actual, TRUE, FALSE)

  group <- data.frame(df, "pred" = pred_t) %>%
  group_by(actual, pred) %>%
  dplyr::summarise(n = n())

  group_b <- filter(group, actual == "benign")

  prop_b <- sum(filter(group_b, pred == TRUE)$n) / sum(group_b$n)
  prop_table[prop_table$threshold == threshold, "prop_true_b"] <- prop_b

  group_m <- filter(group, actual == "malignant")

  prop_m <- sum(filter(group_m, pred == TRUE)$n) / sum(group_m$n)
  prop_table[prop_table$threshold == threshold, "prop_true_m"] <- prop_m
}

prop_table %>%
  gather(x, y, prop_true_b:prop_true_m) %>%
  ggplot(aes(x = threshold, y = y, color = x)) +
    geom_point() +
    geom_line() +
    scale_color_brewer(palette = "Set1") +
    labs(y = "proportion of true predictions",
         color = "b: benign cases\nm: malignant cases")
```



```
h2o.shutdown()
```

If you are interested in more machine learning posts, check out the category listing for **machine_learning** on my blog.

```
sessionInfo()
```

```
## R version 3.3.3 (2017-03-06)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows 7 x64 (build 7601) Service Pack 1
##
## locale:
## [1] LC_COLLATE=English_United States.1252
## [2] LC_CTYPE=English_United States.1252
## [3] LC_MONETARY=English_United States.1252
## [4] LC_NUMERIC=C
## [5] LC_TIME=English_United States.1252
##
## attached base packages:
## [1] stats4    parallel  stats     graphics  grDevices utils     datasets
## [8] methods   base
##
## other attached packages:
##  [1] ggrepel_0.6.5       reshape2_1.4.2      h2o_3.10.3.6
##  [4] corrplot_0.77       plyr_1.8.4          xgboost_0.6-4
##  [7] randomForest_4.6-12  caret_6.0-73         lattice_0.20-34
## [10] doParallel_1.0.10    iterators_1.0.8      foreach_1.4.3
## [13] igraph_1.0.1         tidyr_0.6.1          dplyr_0.5.0
## [16] pcaGoPromoter_1.18.0 Biostrings_2.42.1    XVector_0.14.0
## [19] IRanges_2.8.1        S4Vectors_0.12.1     BiocGenerics_0.20.0
## [22] ellipse_0.3-8        ggplot2_2.2.1.9000
##
## loaded via a namespace (and not attached):
##  [1] Rcpp_0.12.9          class_7.3-14         assertthat_0.1
##  [4] rprojroot_1.2        digest_0.6.12        R6_2.2.0
##  [7] backports_1.0.5      MatrixModels_0.4-1   RSQLite_1.1-2
## [10] evaluate_0.10        e1071_1.6-8          zlibbioc_1.20.0
## [13] lazyeval_0.2.0       minqa_1.2.4          data.table_1.10.4
## [16] SparseM_1.76         car_2.1-4            nloptr_1.0.4
## [19] Matrix_1.2-8         rmarkdown_1.3        labeling_0.3
## [22] splines_3.3.3        lme4_1.1-12          stringr_1.2.0
## [25] RCurl_1.95-4.8       munsell_0.4.3        mgcv_1.8-17
## [28] htmltools_0.3.5      nnet_7.3-12          tibble_1.2
## [31] codetools_0.2-15     MASS_7.3-45          bitops_1.0-6
## [34] ModelMetrics_1.1.0   grid_3.3.3           jsonlite_1.3
## [37] nlme_3.1-131         gtable_0.2.0         DBI_0.6
## [40] magrittr_1.5         scales_0.4.1         stringi_1.1.2
## [43] RColorBrewer_1.1-2   tools_3.3.3          Biobase_2.34.0
## [46] pbkrtest_0.4-6       yaml_2.1.14          AnnotationDbi_1.36.2
## [49] colorspace_1.3-2     memoise_1.0.0        knitr_1.15.1
## [52] quantreg_5.29
```