Initial Practice: Parkinson's Disease

Statistical Learning with Deep Artificial Neural Networks

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Contents

1 Introduction

We are working on a dataset describing Parkinson's disease. Click here for more information regarding the dataset. In short, the dataset is composed of a range of biomedical voice measurements from 42 people with early-stage Parkinson's disease recruited to a six-month trial of a telemonitoring device for remote symptom progression monitoring.

The main objective is to predict the severity of Parkinson's disease based on the data. More details are given in the following.

2 Load the Parkinsons Data

```
data <- read.csv("parkinsons_updrs.data")
str(data)
```

```
#> 'data.frame':    5875 obs. of  22 variables:
#>  $ subject.     : int  1 1 1 1 1 1 1 1 1 1 ...
#>  $ age          : int  72 72 72 72 72 72 72 72 72 72 ...
#>  $ sex          : int  0 0 0 0 0 0 0 0 0 0 ...
#>  $ test_time    : num  5.64 12.67 19.68 25.65 33.64 ...
#>  $ motor_UPDRS  : num  28.2 28.4 28.7 28.9 29.2 ...
#>  $ total_UPDRS  : num  34.4 34.9 35.4 35.8 36.4 ...
#>  $ Jitter...    : num  0.00662 0.003 0.00481 0.00528 0.00335 0.00353 0.00422 0.00476 0.00432 0.00496
#>  $ Jitter.Abs.  : num  3.38e-05 1.68e-05 2.46e-05 2.66e-05 2.01e-05 ...
#>  $ Jitter.RAP   : num  0.00401 0.00132 0.00205 0.00191 0.00093 0.00119 0.00212 0.00226 0.00156 0.002
#>  $ Jitter.PPQ5  : num  0.00317 0.0015 0.00208 0.00264 0.0013 0.00159 0.00221 0.00259 0.00207 0.00253
#>  $ Jitter.DDP   : num  0.01204 0.00395 0.00616 0.00573 0.00278 ...
#>  $ Shimmer      : num  0.0256 0.0202 0.0168 0.0231 0.017 ...
#>  $ Shimmer.dB.  : num  0.23 0.179 0.181 0.327 0.176 0.214 0.445 0.212 0.371 0.31 ...
#>  $ Shimmer.APQ3 : num  0.01438 0.00994 0.00734 0.01106 0.00679 ...
#>  $ Shimmer.APQ5 : num  0.01309 0.01072 0.00844 0.01265 0.00929 ...
#>  $ Shimmer.APQ11: num  0.0166 0.0169 0.0146 0.0196 0.0182 ...
#>  $ Shimmer.DDA  : num  0.0431 0.0298 0.022 0.0332 0.0204 ...
#>  $ NHR          : num  0.0143 0.0111 0.0202 0.0278 0.0116 ...
#>  $ HNR          : num  21.6 27.2 23 24.4 26.1 ...
#>  $ RPDE         : num  0.419 0.435 0.462 0.487 0.472 ...
#>  $ DFA          : num  0.548 0.565 0.544 0.578 0.561 ...
#>  $ PPE          : num  0.16 0.108 0.21 0.333 0.194 ...
```

```
summary(data)
```

```
#>     subject.          age            sex           test_time
#>  Min.   : 1.00   Min.   :36.0   Min.   :0.0000   Min.   : -4.263
#>  1st Qu.:10.00   1st Qu.:58.0   1st Qu.:0.0000   1st Qu.: 46.847
#>  Median :22.00   Median :65.0   Median :0.0000   Median : 91.523
#>  Mean   :21.49   Mean   :64.8   Mean   :0.3178   Mean   : 92.864
#>  3rd Qu.:33.00   3rd Qu.:72.0   3rd Qu.:1.0000   3rd Qu.:138.445
#>  Max.   :42.00   Max.   :85.0   Max.   :1.0000   Max.   :215.490
#>   motor_UPDRS      total_UPDRS      Jitter...         Jitter.Abs.
#>  Min.   : 5.038   Min.   : 7.00   Min.   :0.000830   Min.   :2.250e-06
#>  1st Qu.:15.000   1st Qu.:21.37   1st Qu.:0.003580   1st Qu.:2.244e-05
#>  Median :20.871   Median :27.58   Median :0.004900   Median :3.453e-05
#>  Mean   :21.296   Mean   :29.02   Mean   :0.006154   Mean   :4.403e-05
#>  3rd Qu.:27.596   3rd Qu.:36.40   3rd Qu.:0.006800   3rd Qu.:5.333e-05
#>  Max.   :39.511   Max.   :54.99   Max.   :0.099990   Max.   :4.456e-04
```

```
#>    Jitter.RAP        Jitter.PPQ5         Jitter.DDP          Shimmer
#>  Min.   :0.000330   Min.   :0.000430   Min.   :0.000980   Min.   :0.00306
#>  1st Qu.:0.001580   1st Qu.:0.001820   1st Qu.:0.004730   1st Qu.:0.01912
#>  Median :0.002250   Median :0.002490   Median :0.006750   Median :0.02751
#>  Mean   :0.002987   Mean   :0.003277   Mean   :0.008962   Mean   :0.03404
#>  3rd Qu.:0.003290   3rd Qu.:0.003460   3rd Qu.:0.009870   3rd Qu.:0.03975
#>  Max.   :0.057540   Max.   :0.069560   Max.   :0.172630   Max.   :0.26863
#>   Shimmer.dB.      Shimmer.APQ3      Shimmer.APQ5     Shimmer.APQ11
#>  Min.   :0.026   Min.   :0.00161   Min.   :0.00194   Min.   :0.00249
#>  1st Qu.:0.175   1st Qu.:0.00928   1st Qu.:0.01079   1st Qu.:0.01566
#>  Median :0.253   Median :0.01370   Median :0.01594   Median :0.02271
#>  Mean   :0.311   Mean   :0.01716   Mean   :0.02014   Mean   :0.02748
#>  3rd Qu.:0.365   3rd Qu.:0.02057   3rd Qu.:0.02375   3rd Qu.:0.03272
#>  Max.   :2.107   Max.   :0.16267   Max.   :0.16702   Max.   :0.27546
#>   Shimmer.DDA           NHR                HNR              RPDE
#>  Min.   :0.00484   Min.   :0.000286   Min.   : 1.659   Min.   :0.1510
#>  1st Qu.:0.02783   1st Qu.:0.010955   1st Qu.:19.406   1st Qu.:0.4698
#>  Median :0.04111   Median :0.018448   Median :21.920   Median :0.5423
#>  Mean   :0.05147   Mean   :0.032120   Mean   :21.680   Mean   :0.5415
#>  3rd Qu.:0.06173   3rd Qu.:0.031463   3rd Qu.:24.444   3rd Qu.:0.6140
#>  Max.   :0.48802   Max.   :0.748260   Max.   :37.875   Max.   :0.9661
#>       DFA              PPE
#>  Min.   :0.5140   Min.   :0.02198
#>  1st Qu.:0.5962   1st Qu.:0.15634
#>  Median :0.6436   Median :0.20550
#>  Mean   :0.6532   Mean   :0.21959
#>  3rd Qu.:0.7113   3rd Qu.:0.26449
#>  Max.   :0.8656   Max.   :0.73173
```

3 Description of the Variables

As we have seen above, the dataset contains 5875 rows, i.e. 5875 measurements. The columns consist of **patient ID**, **age**, **sex**, **time interval since enrollment date**, **motor_UPDRS**, **total_UPDRS** and 16 voice biomedical measurements. The variables are the following

- subject. - The patient ID. Integer that uniquely identifies each subject.
- age - Age of each subject.
- sex - Gender of the subject; '0' = male and '1' = female.
- test_time - Time since recruitment into the trial. The integer part is the number of days since recruitment.
- motor_UPDRS - Clinician's motor UPDRS score, linearly interpolated.
- ctotal_UPDRS - Clinician's total UPDRS score, linearly interpolated.
- Jitter(%), Jitter(Abs), Jitter:RAP, Jitter:PPQ5, Jitter:DDP - Several measures of variation in fundamental frequency.
- Shimmer, Shimmer(dB), Shimmer:APQ3, Shimmer:APQ5, Shimmer:APQ11, Shimmer:DDA - Several measures of variation in amplitude.
- NHR, HNR - Two measures of ratio of noise to tonal components in the voice.
- RPDE - A nonlinear dynamical complexity measure.
- DFA - Signal fractal scaling exponent.
- PPE - A nonlinear measure of fundamental frequency variation.

As noted, the objective is to predict the severity of the disease, where severity is defined based on the variable **total_UPDRS**: The disease is severe if **total_UPDRS $>$ 25**. This variable is created below.

4 Create the Binary Variable of Parkinson's Severity

```
data$severity <- data$total_UPDRS > 25
dim(data)
```

```
#> [1] 5875   23
```

```
summary(data$severity)
```

```
#>    Mode   FALSE    TRUE
#> logical    2188    3687
```

5 Normalization

The variables of the 16 voice measurements are normalized by means of the min-max transformation.

```
normalize <- function(x) {
    return((x- min(x))/(max(x)-min(x)))
}

for (i in 1:16){
  data[, 6+i] <- normalize(data[,6+i])
}

summary(data)
```

```
#>     subject.          age            sex           test_time
#>  Min.   : 1.00   Min.   :36.0   Min.   :0.0000   Min.   : -4.263
#>  1st Qu.:10.00   1st Qu.:58.0   1st Qu.:0.0000   1st Qu.: 46.847
#>  Median :22.00   Median :65.0   Median :0.0000   Median : 91.523
#>  Mean   :21.49   Mean   :64.8   Mean   :0.3178   Mean   : 92.864
#>  3rd Qu.:33.00   3rd Qu.:72.0   3rd Qu.:1.0000   3rd Qu.:138.445
#>  Max.   :42.00   Max.   :85.0   Max.   :1.0000   Max.   :215.490
#>   motor_UPDRS      total_UPDRS      Jitter...         Jitter.Abs.
#>  Min.   : 5.038   Min.   : 7.00   Min.   :0.00000   Min.   :0.00000
#>  1st Qu.:15.000   1st Qu.:21.37   1st Qu.:0.02773   1st Qu.:0.04553
#>  Median :20.871   Median :27.58   Median :0.04104   Median :0.07281
#>  Mean   :21.296   Mean   :29.02   Mean   :0.05369   Mean   :0.09423
#>  3rd Qu.:27.596   3rd Qu.:36.40   3rd Qu.:0.06021   3rd Qu.:0.11523
#>  Max.   :39.511   Max.   :54.99   Max.   :1.00000   Max.   :1.00000
#>    Jitter.RAP       Jitter.PPQ5        Jitter.DDP         Shimmer
#>  Min.   :0.00000   Min.   :0.00000   Min.   :0.00000   Min.   :0.00000
#>  1st Qu.:0.02185   1st Qu.:0.02011   1st Qu.:0.02185   1st Qu.:0.06047
#>  Median :0.03356   Median :0.02980   Median :0.03361   Median :0.09207
#>  Mean   :0.04645   Mean   :0.04118   Mean   :0.04650   Mean   :0.11664
#>  3rd Qu.:0.05174   3rd Qu.:0.04383   3rd Qu.:0.05179   3rd Qu.:0.13816
#>  Max.   :1.00000   Max.   :1.00000   Max.   :1.00000   Max.   :1.00000
#>   Shimmer.dB.      Shimmer.APQ3      Shimmer.APQ5     Shimmer.APQ11
#>  Min.   :0.0000   Min.   :0.00000   Min.   :0.00000   Min.   :0.00000
#>  1st Qu.:0.0716   1st Qu.:0.04762   1st Qu.:0.05361   1st Qu.:0.04827
#>  Median :0.1091   Median :0.07507   Median :0.08481   Median :0.07407
#>  Mean   :0.1369   Mean   :0.09652   Mean   :0.11027   Mean   :0.09155
#>  3rd Qu.:0.1629   3rd Qu.:0.11775   3rd Qu.:0.13215   3rd Qu.:0.11073
#>  Max.   :1.0000   Max.   :1.00000   Max.   :1.00000   Max.   :1.00000
#>   Shimmer.DDA           NHR               HNR              RPDE
```

```
#>  Min.   :0.00000   Min.   :0.00000   Min.   :0.0000   Min.   :0.0000
#>  1st Qu.:0.04758   1st Qu.:0.01426   1st Qu.:0.4900   1st Qu.:0.3911
#>  Median :0.07507   Median :0.02428   Median :0.5594   Median :0.4800
#>  Mean   :0.09650   Mean   :0.04256   Mean   :0.5528   Mean   :0.4790
#>  3rd Qu.:0.11775   3rd Qu.:0.04168   3rd Qu.:0.6291   3rd Qu.:0.5681
#>  Max.   :1.00000   Max.   :1.00000   Max.   :1.0000   Max.   :1.0000
#>       DFA              PPE          severity
#>  Min.   :0.0000   Min.   :0.0000   Mode :logical
#>  1st Qu.:0.2336   1st Qu.:0.1893   FALSE:2188
#>  Median :0.3685   Median :0.2586   TRUE :3687
#>  Mean   :0.3959   Mean   :0.2784
#>  3rd Qu.:0.5612   3rd Qu.:0.3417
#>  Max.   :1.0000   Max.   :1.0000
```

6 Separation into Train and Test Data

I will use (pseudo-) random sampling to separate the data into a training and test set.

```
#set.seed(1)
ratio <- 0.7
sample.size <- floor(nrow(data) * ratio)
train.indices <- sample(1:nrow(data), size = sample.size)
train <- data[train.indices, ]
test <- data[-train.indices, ]

x_train <- data.matrix(train[,-23])
y_train <- to_categorical(train[, 23], num_classes = 2)
```

```
#> Loaded Tensorflow version 2.7.1
```

```
x_test <- data.matrix(test[,-23])
y_test <- to_categorical(test[, 23], num_classes = 2)
```

7 Implementation of a Dense DNN

A dense deep neural network (DNN) for severity prediction is made. It has two hidden layers, with 10 nodes in each hidden layer. I have implemented two variants of this DNN; variant A has two output nodes, while variant B has only one output node.

7.1 Variant A: Two Output Nodes

Since we have two output nodes in this variant, we should use the *softmax* activation function in the output and the *categorical_crossentropy* loss function.

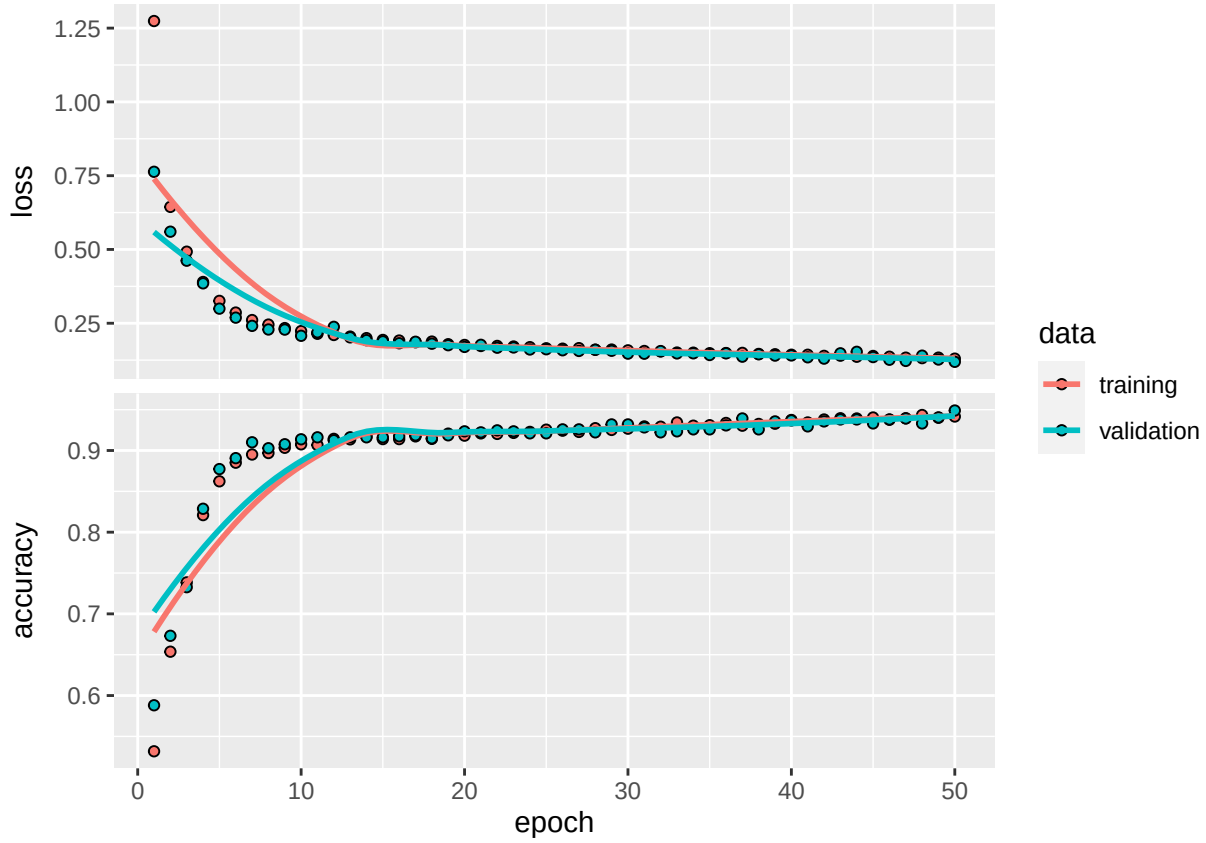
```
#set.seed(1)
# defining the model and layers
model <- keras_model_sequential() %>%
  layer_dense(units = 10, activation = 'relu', input_shape = c(ncol(x_train))) %>%
  layer_dense(units = 10, activation = 'relu') %>%
  layer_dense(units = ncol(y_train), activation = 'softmax')

summary(model)
```

```
#> Model: "sequential"
#> ________________________________________________________________________________
```

```
#>  Layer (type)                       Output Shape                    Param #
#> ================================================================================
#>  dense_2 (Dense)                    (None, 10)                      230
#>
#>  dense_1 (Dense)                    (None, 10)                      110
#>
#>  dense (Dense)                      (None, 2)                       22
#>
#> ================================================================================
#> Total params: 362
#> Trainable params: 362
#> Non-trainable params: 0
#> --------------------------------------------------------------------------------
```

```
# compile (define loss and optimizer)
model %>% compile(loss = 'categorical_crossentropy',
                  optimizer = optimizer_rmsprop(),
                  metrics = c('accuracy'))
# train (fit)
history <- model %>% fit(data.matrix(x_train), y_train, epochs = 50,
                batch_size = 128, validation_split = 0.2)
# plot
plot(history)
```

```
#> `geom_smooth()` using formula 'y ~ x'
```




```
# evaluate on training data.
model %>% evaluate(x_train, y_train)
```

```
#>      loss  accuracy
#> 0.1233088 0.9443094
```

```
# evaluate on test data.
model %>% evaluate(x_test, y_test)
```

```
#>      loss  accuracy
#> 0.1299942 0.9427113
```

7.2 Variant B: One Output Node

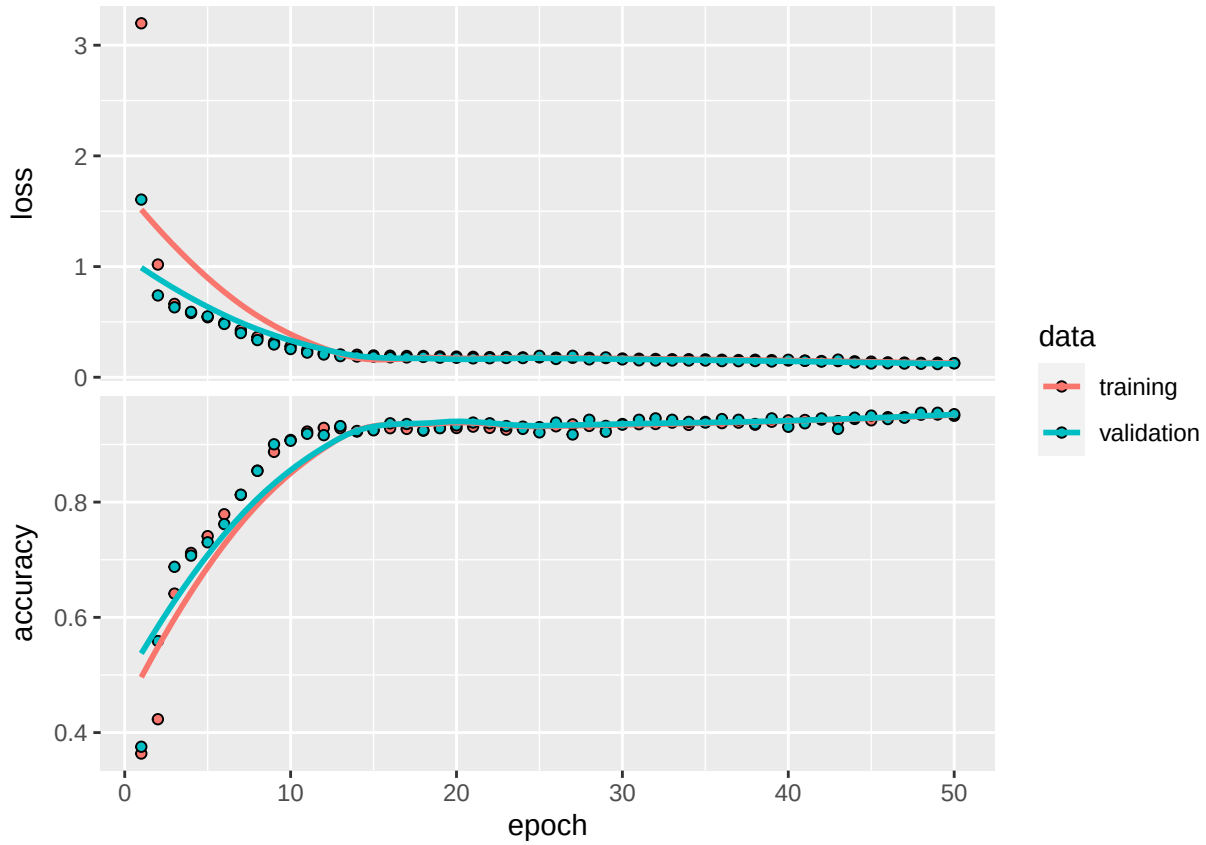
Since we have one output nodes in this variant, we should use the *sigmoid* activation function in the output and the *binary_crossentropy* loss function.

```
set.seed(1)
# defining the model and layers
model2 <- keras_model_sequential() %>%
  layer_dense(units = 10, activation = 'relu', input_shape = c(ncol(x_train))) %>%
  layer_dense(units = 10, activation = 'relu') %>%
  layer_dense(units = 1, activation = 'sigmoid')

summary(model2)
```

```
#> Model: "sequential_1"
#> ________________________________________________________________________________
#>  Layer (type)                       Output Shape                    Param #
#> ================================================================================
#>  dense_5 (Dense)                    (None, 10)                      230
#>
#>  dense_4 (Dense)                    (None, 10)                      110
#>
#>  dense_3 (Dense)                    (None, 1)                       11
#>
#> ================================================================================
#> Total params: 351
#> Trainable params: 351
#> Non-trainable params: 0
#> ________________________________________________________________________________
```

```
y_train2 <- as.numeric(data.matrix(train[,23]))
y_test2 <- as.numeric(data.matrix(test[,23]))

# compile (define loss and optimizer)
model2 %>% compile(loss = 'binary_crossentropy',
                   optimizer = optimizer_rmsprop(),
                   metrics = c('accuracy'))
# train (fit)
history2 <- model2 %>% fit(data.matrix(x_train), y_train2, epochs = 50,
              batch_size = 128, validation_split = 0.2)
# plot
plot(history2)
```

```
#> `geom_smooth()` using formula 'y ~ x'
```




```
# evaluate on training data.
model2 %>% evaluate(x_train, y_train2)
```

```
#>      loss  accuracy
#> 0.1274880 0.9552529
```

```
# evaluate on testing data.
model2 %>% evaluate(x_test, y_test2)
```

```
#>      loss  accuracy
#> 0.1287149 0.9534883
```

Note that the accuracy is reported as being higher for the test set compared to the training set in both variants (in many runs). This should not happen, but it looks like it does not happen when I do not min-max transform the data. Why? I have not been able to find an error, e.g. in the transform or in the test/train split.

8 Predictions

8.1 Predictions for Variant A

```
y_pred <- model %>% predict(x_test) %>% k_argmax()
y_pred <- as.array(y_pred)
(tab <- table("Predictions" = y_pred, "Labels" = test[, 23]))
```

```
#>            Labels
#> Predictions FALSE TRUE
#>           0   628   46
```

```
#>           1    55 1034
```

```
# accuracy in predictions (as shown with the "evaluate" above).
(tab[1]+tab[4])/sum(tab)
```

```
#> [1] 0.9427113
```

8.2 Predictions for Variant B

```
# Predictions for one output node
y_pred2 <- model2 %>% predict(x_test) %>% `>`(0.5) %>% k_cast("int32")
y_pred2 <- as.array(y_pred2)
(tab2 <- table("Predictions" = y_pred2, "Labels" = test[, 23]))
```

```
#>            Labels
#> Predictions FALSE TRUE
#>           0   622   21
#>           1    61 1059
```

```
# accuracy in predictions (as shown with the "evaluate" above).
(tab2[1]+tab2[4])/sum(tab2)
```

```
#> [1] 0.9534884
```