DRUMLR Tutorial

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Contents

0.1 Set up

To install the DRUMLR package into R you will need to download the DRUMLRv01_0.1.0.tar.gz and Example Models Folder from Github. Then run the following line of code. You will need the path to the download location of the DRUMLRv01_0.1.0.tar.gz to do this (this will usually be "C:/Users/Username/Downloads/DRUMLRv01_0.1.0.tar.gz" where your Username is in the place of "Username").

```
install.packages("C:/Users/Username/Downloads/DRUMLRv01_0.1.0.tar.gz",
                 repos = NULL,
                 type ="source")
```

1 Building DRUML models with DRUMLR

Load Libraries

```
library(tidyverse)
library(DRUMLR)
```

1.1 Generate markers

Import and scale input data. Then use the processed data to build markers for DRUMLR models.

```
#import datasets
df_input <- Input_data %>% scale(center = T, scale = T)
df_response <- Response_data

#Generate EMDRs
markers <-
  DRUMLR::BuildEMDR(
    df_input = Input_data,
    df_response = t(df_response),
    drugs = drugs,
    computational_load = 0.8
  )
```

1.2 Build Models

function .BuildModels contains the paramaters used for the models

```
Model_info <-
  DRUMLR::BuildDRUMLs(
    df_input = df_input_aml,
    .marker_database = markers,
    input_type = "aml_phospho",
    save_path = "~/DRUML_models",
    save_csv = T,
    models = "all",
    df_response = df_response,
    drugs = drugs,
    computational_load = 0.8
  )
```

1.3 Verification with External Data

Prediction of verification data shown in verification data example.

```
df_validation <- external_data

df_validatiaon_dist <-
  DRUMLR::DrugMarkerEnrichment(df = df_validation, marker_database = markers)

df_predictions <-
  DRUMLR::PredictDRUML(df_distance = df_validatiaon_dist,
                       models = "all",
                       models_dir = "~/DRUML_models")
```

2 Verification of Gerdes et al DRUML models using clinical AML data

Load Libraries

```
library(DRUMLR)
library(tidyverse)
library(survival)
```

2.1 Import Internal Data

Import internal DRUML data for verification.

```
#Import and scale Verification Phosphoproteomic input data from clinical aml samples
df_input <- DRUMLR:::Primary_AML_phospho_data

#Import survival and molecular classification data for clinical AML samples
df_survival <-DRUMLR:::Primary_AML_survival_data
```

2.2 Calculate Fistance values

In this example we will predict the sensitivity of clinical_phosphoproteomics samples to Cytarabine. To generate rankings peptide abundance values are scaled for each sample. Distance values for these data are generated using the DRUMLR::DrugMarkerEnrichment() function.

The markers_databases which can be used in for this are:

- Phosphoproteomics:
  - DRUMLR:::phospho_aml_markers.
  - DRUMLR:::phospho_solid_markers.
- Proteomic:
  - DRUMLR:::prot_aml_markers.
  - DRUMLR:::prot_solid_markers.

In this care we will be using phospho_aml_markers

```
# Get relevant marker database. For this example we are using phosphoproteomics
# data
markers <- DRUMLR:::phospho_aml_markers

# Carry out Drug Marker Enrichment on the data using the relevant makers database
df_distance <- DRUMLR::DrugMarkerEnrichment(df = df_input, marker_database = markers)
```

2.3 AAC prediction using Gerdes et al models

To predict Drug Sensitivity you will need to state the path to the folder containing all of the Example Models. In this example we are predicting Cytarabine sensitivity using partial list squares (pls), principal components regression (pcr) and random forest (rf) models.

```
#To predict Drug Sensitivity you will need to state the path to the folder containing all of the Models

predictions <- DRUMLR::PredictDRUML_example(df_distance = df_distance,
                          input_type = "phospho",
                          cancer_type = "aml",
                          models = c("rf","pcr","pls"),
                          drugs = "Cytarabine",
```

```
                          models_dir = "Example_Models"
                          )
```

2.4 Rearrange Prediction output for graphs

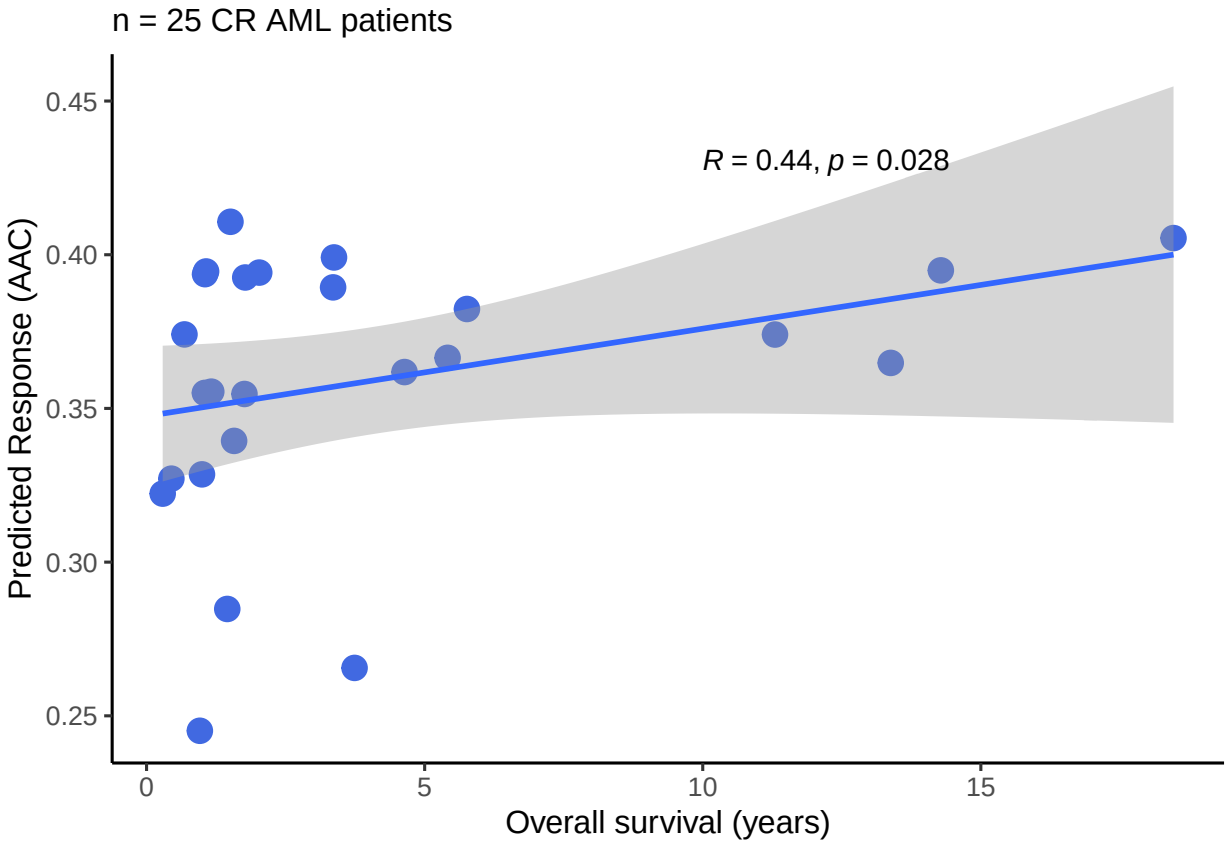
Useful code for reshaping prediction results for ggplot2 based graphs.

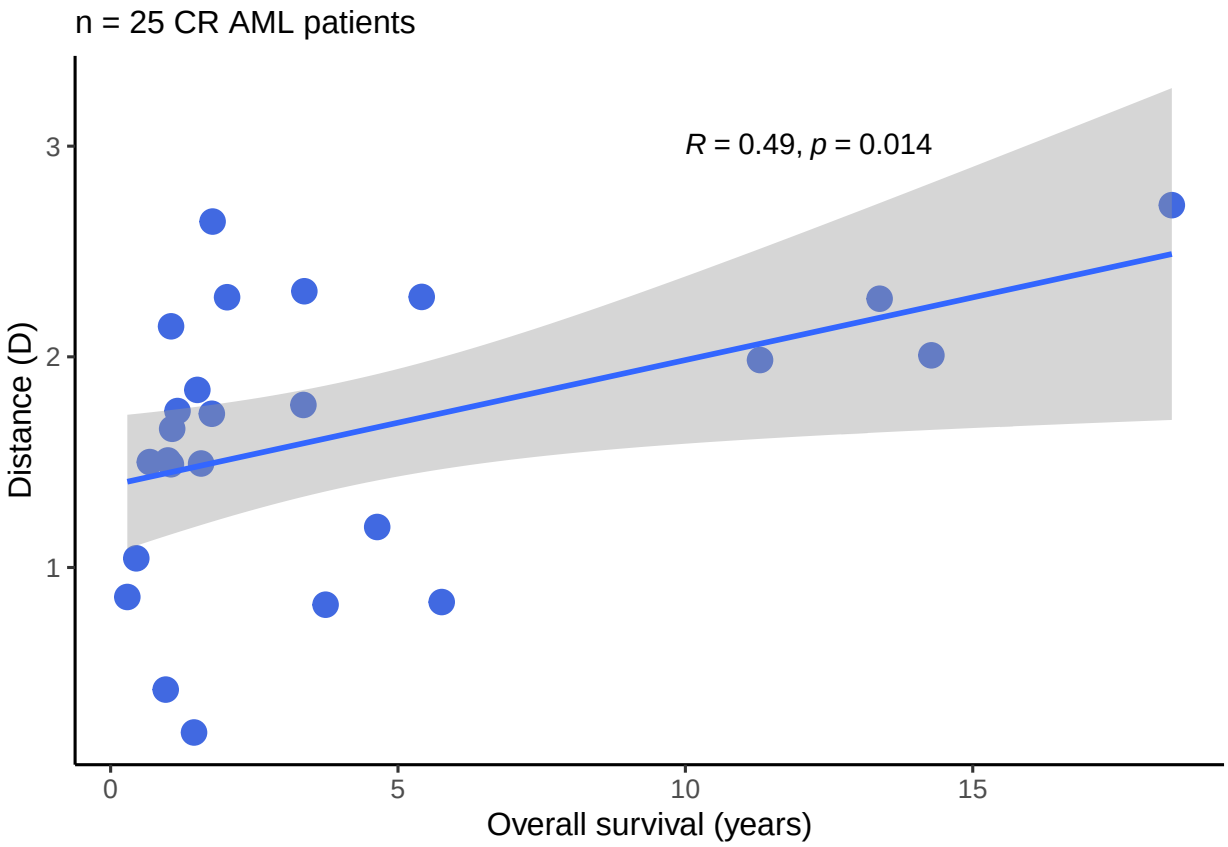
```
# Get average of predictions
df_prediction2 <- t(predictions) %>% data.frame()
df_prediction2["Cytarabine_aml_median", ] <- apply(df_prediction2, MARGIN = 2, median)
# label Predictions outputs
df_labs <- strsplit(rownames(df_prediction2), "_") %>% data.frame() %>% t()
colnames(df_labs) <- c("drug", "tissue", "model")

# labeled ML predictions
df_prediction2 <- cbind(df_labs[, "model"], df_prediction2) %>% reshape2::melt()
colnames(df_prediction2) <- c("model", "Vial.ID", "aac")

# Add survival and D data to dataframe
df_prediction2 <- merge.data.frame(df_prediction2, df_survival, by = "Vial.ID")
df_prediction2$D <- df_distance["Cytarabine", df_prediction2$Vial.ID] %>% as.vector()
```

2.5 Verification graphs

2.5.1 Correlation of Predicted AAC with Patient Survival

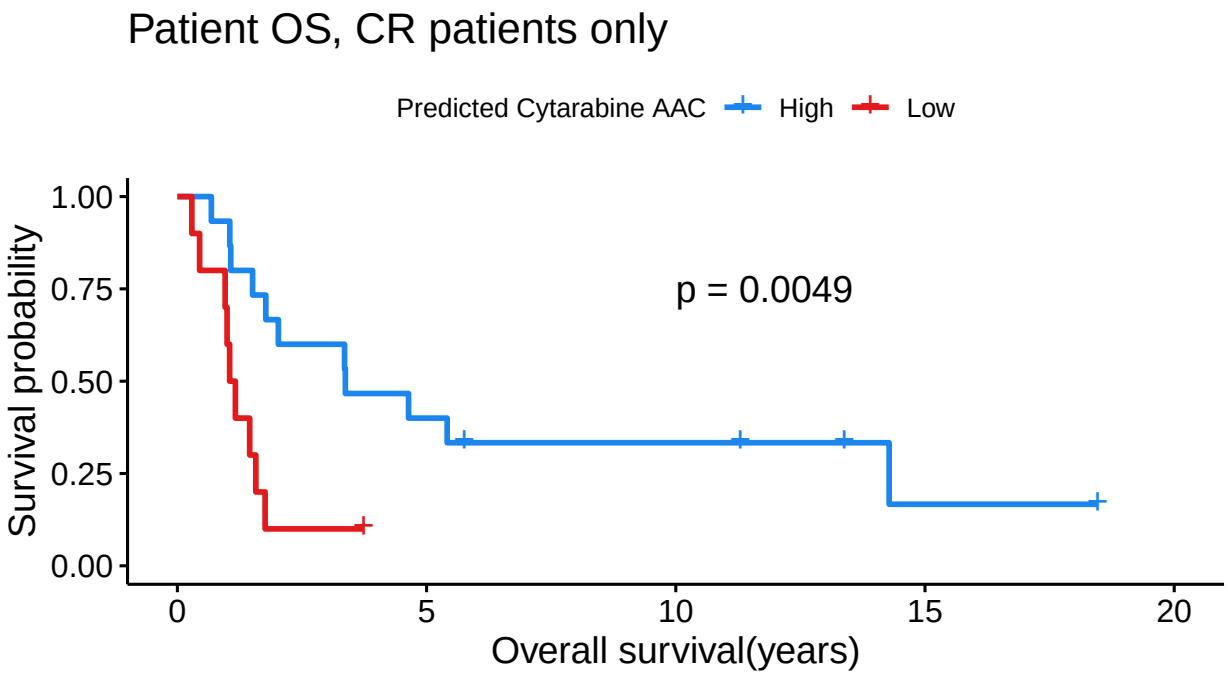
Scatter graphs demonstrating the correlation between median predicted AAC values against patient survival rate in years.



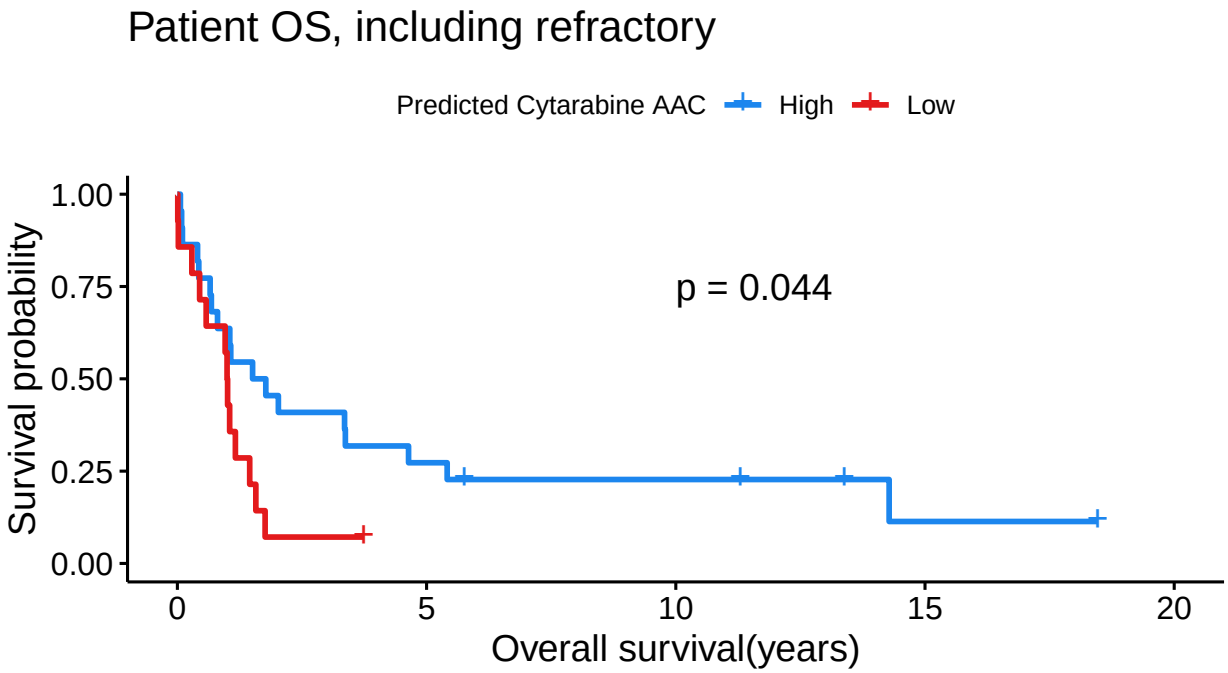

n = 25 CR AML patients
R = 0.49, p = 0.014
Distance (D)
3
2
1
0
5
10
15
Overall survival (years)

2.5.2 Make Kaplain Meyer classifications

Patients were split into "high" and "low" groups using mean AAC and D values.



	records	*rmean	median	0.95LCL	0.95UCL
high	15	7.12	3.37	1.77	NA
low	10	2.82	1.11	0.96	NA



	records	*rmean	median	0.95LCL	0.95UCL
high	22	4.97	1.64	0.8	5.41
low	14	2.13	1	0.58	1.76