Vignette PlasmodeSim

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Welcome to the vignette about the R package PlasmodeSim. This package is still under development. This package goal is to simulate new outcomes for real patients data. The outcome will follow model you specify.

Installing plasmodeSim using remotes

One can easily install the package using `remotes`, run:

```
install.packages("remotes")
remotes::install_github("GidiusVanDeKamp/PlasmodeSim")
```

Logistic Regression

Setting up

To start we need a plpModel and plpData. For information how to obtain these one can look at: https://ohdsi.github.io/PatientLevelPrediction/articles/BuildingPredictiveModels.html In this documents we load them from a save file:

```
plpResultLogistic <- PatientLevelPrediction::loadPlpResult( "yourpathForPlpResult")
plpData <- PatientLevelPrediction::loadPlpData( "yourPathForPlpData" )
```

Example 1 Simulate from a plpModel

In this example we obtain new outcomes following a fitted logistic model. We start from a plpModel, then run predictPlp. At last we generate new outcomes with the function `newOutcomes` that uses the plpPrediction.

```
plpModelLog <- plpResultLogistic$model

plpPrediction <- PatientLevelPrediction::predictPlp(
  plpModel = plpModelLog,
  plpData = plpData,
  population = plpData$cohorts
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.196 secs
## Prediction took 0.182 secs
```

When running the function predictPlp it returns some information.

```
newOut <- PlasmodeSim::newOutcomes(
  noPersons = 200,
  props = plpPrediction
)
head(newOut)
```

```
##   rowId outcomeCount
## 1    11            1
## 2    16            0
## 3    22            0
## 4    28            0
## 5    39            0
## 6    49            0
```

The rowId in the output of `newOutcomes` are the rowId of patients that are drawn randomly with the same probability, the patients could be drawn multiple times. If a rowId happens to be in the output twice they can have a different outcome. The function `newOutcomes` needs a data set that contains the columns `rowId` and `value`. The column called `value` contains the probabilities used in generating the new outcomes.

Example 2 simulation from unfittedmodel

We here we show how to simulate outcomes from an unfitted logistic model. We use the function `makeLogisiticModel` to specify a logistic model.

```
Parameters <- plpModelLog$model$coefficients
UnfittedParameters <- Parameters
UnfittedParameters[1,1] <- -0.4
UnfittedParameters[3:5,1] <- 0.4
head(UnfittedParameters)
```

```
##   betas covariateIds
## 1  -0.4  (Intercept)
## 2   0.0         6003
## 3   0.4         8003
## 4   0.4         9003
## 5   0.4      8507001
## 6   0.0     28060210
```

For the logistic model it is necessary that the parameters are stored in a dataset with a column called `betas` and a column called `covariateIds`. The function `makeLogisitcModel` makes a plpModel from the specified parameters.

```
plpModelunfitted <- PlasmodeSim::makeLogisticModel(UnfittedParameters)
newprobs <- PatientLevelPrediction::predictPlp(
  plpModel = plpModelunfitted,
  plpData = plpData,
  population = plpData$cohorts
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.174 secs
## Prediction took 0.177 secs
```

```
newOut <- PlasmodeSim::newOutcomes(
  noPersons = 2000,
  props = newprobs
)
head(newOut)
```

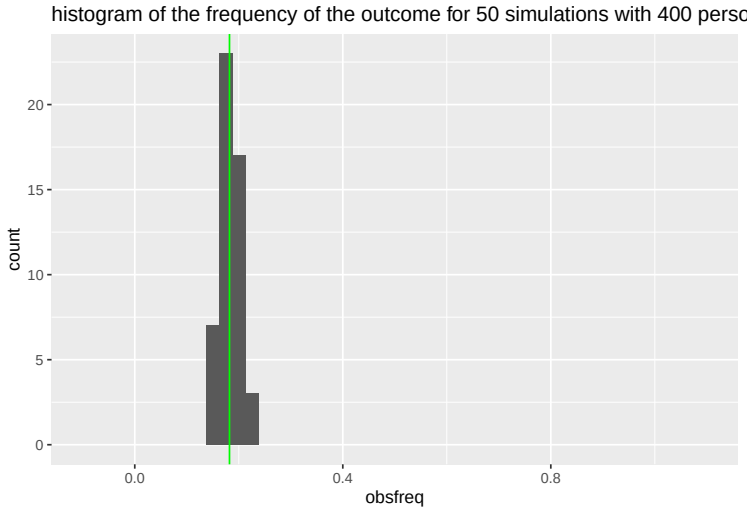
```
##   rowId outcomeCount
## 1     1            1
## 2     2            0
## 3     3            0
## 4     3            1
## 5     3            0
## 6     6            1
```

Visual simulations

The function `visualOutcome` simulates new data and then plots the frequency of the outcome. Right now the function `visualOutcome` only works for a logistic model. The green line in the plots is the average outcome in the original dataset.

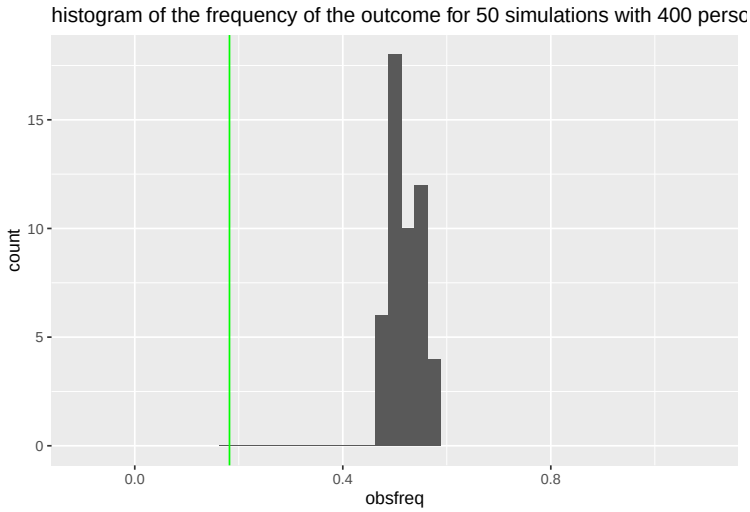
```
PlasmodeSim::visualOutcome(
  plpData = plpData,
  noSimulations = 50,
  noPersons = 400,
  parameters = Parameters
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.184 secs
## Prediction took 0.171 secs
```




```
PlasmodeSim::visualOutcome(
  plpData = plpData,
  noSimulations = 50,
  noPersons = 400,
  parameters = UnfittedParameters
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.186 secs
## Prediction took 0.173 secs
```



Here we have plotted 50 times the frequency of the outcome for a simulated dataset with 200 people. We can see that the outcome count for the fitted parameters is similar as in the original dataset, but when changing the parameters the outcome count also changes.

Visual of a specific covariate

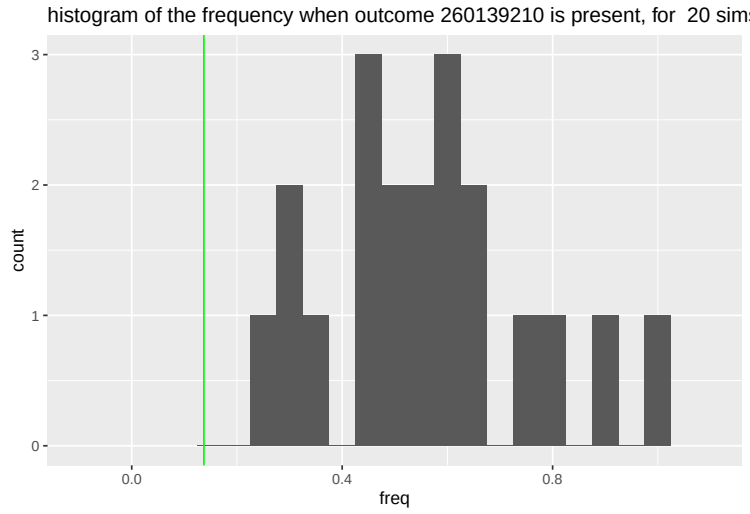
Say we are interested in the outcomes of a group with a specific covariate. Here we picked the third covariate in the model to visualise.

```
covariateIdToStudy<- plpResultLogistic$covariateSummary$covariateId[4]
UnfittedParameters[4,]
```

```
##   betas covariateIds
## 4   0.4         9003
```

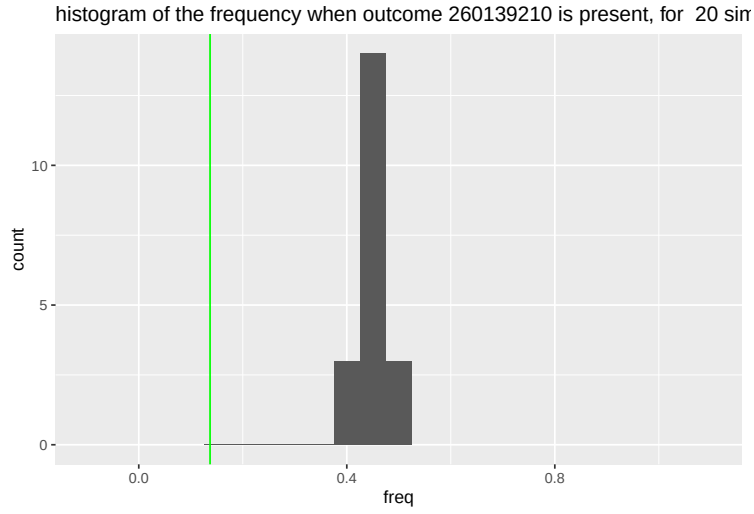
```
PlasmodeSim::visualOutcomeCovariateId(
  plpData=plpData,
  studyCovariateId= covariateIdToStudy,
  noSimulations = 20,
  noPersons = 200,
  parameters= UnfittedParameters
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.194 secs
## Prediction took 0.187 secs
```



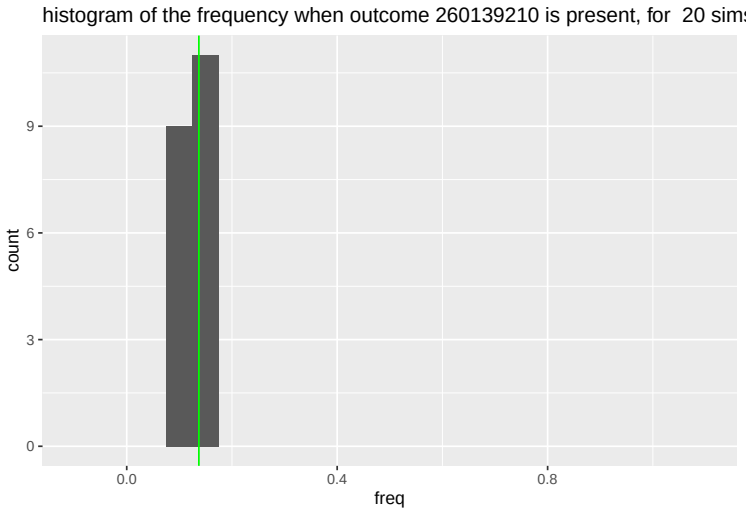

```
PlasmodeSim::visualOutcomeCovariateId2(
  plpData=plpData,
  restrictToCovariateId= covariateIdToStudy,
  noSimulations = 20,
  noPersons= 200,
  parameters= UnfittedParameters
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.188 secs
## Prediction took 0.174 secs
```




```
PlasmodeSim::visualOutcomeCovariateId2(
  plpData=plpData,
  restrictToCovariateId= covariateIdToStudy,
  noSimulations = 20,
  noPersons= 200,
  parameters= Parameters
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.187 secs
## Prediction took 0.173 secs
```



As one can see `visualOutcomeCovariateId` and `visualOutcomeCovariateId2` are very similiar, they both calculate and plot the frequency for a group with a specific covariate present. The small difference is that `visualOutcomeCovariateId` filters a newly simulated dataset set to only keep the patients where the covariate is present, and `visualOutcomeCovariateId2` only simulates new outcomes for patients that have the covariate present. We see they are almost the identical only `visualOutcomeCovariateId2` is spread out less because the groups for calculating the frequency with are larger. Again we see that when picking the fitted parameters the outcome count for patients with a specific covariate is similar as it was in the original data set.

Survival times

In this part we will show how to simulate new survival times. For simulating new censored survival times we need more than one probability, we use the baselinehazard, stored in the a plpModel.

Loading the plpData

The first step is to load the data where we will simulate new outcomes for. Here we use the package eunomia for a accessing some data set.

```
connectionDetails <- Eunomia::getEunomiaConnectionDetails()

Eunomia::createCohorts(
  connectionDetails = connectionDetails,
  cdmDatabaseSchema = 'main',
  cohortDatabaseSchema = 'main',
  cohortTable = 'cohort'
)
```

```
## Creating cohort: Celecoxib
##   |                                                                      |
```

```
## Creating cohort: Diclofenac
##   |                                                                      |
## Creating cohort: GiBleed
##   |                                                                      |
## Creating cohort: NSAIDs
##   |                                                                      |
## Cohorts created in table main.cohort

##   cohortId       name
## 1        1  Celecoxib
## 2        2 Diclofenac
## 3        3    GiBleed
## 4        4     NSAIDs
##                                                                                 description
## 1    A simplified cohort definition for new users of celecoxib, designed specifically for Eunomia.
## 2    A simplified cohort definition for new users ofdiclofenac, designed specifically for Eunomia.
## 3 A simplified cohort definition for gastrointestinal bleeding, designed specifically for Eunomia.
## 4       A simplified cohort definition for new users of NSAIDs, designed specifically for Eunomia.
##   count
## 1  1844
## 2   850
## 3   479
## 4  2694
```

```
databaseDetails <- PatientLevelPrediction::createDatabaseDetails(
  connectionDetails = connectionDetails,
  cdmDatabaseId = "eunomia",
  cdmDatabaseSchema = 'main',
  cdmDatabaseName = 'Eunomia',
  cohortDatabaseSchema = 'main',
  cohortTable = 'cohort',
  target = 4,
  outcomeDatabaseSchema = 'main',
  outcomeTable = 'cohort',
  outcomeId = 3,
  cdmVersion = 5
)

covariateSettings <- FeatureExtraction::createCovariateSettings(
  useDemographicsGender = TRUE,
  useDemographicsAgeGroup = TRUE,
  useConditionGroupEraLongTerm = TRUE,
  useDrugGroupEraLongTerm = TRUE,
  endDays = -1,
  longTermStartDays = -365
)

restrictPlpDataSettings <- PatientLevelPrediction::createRestrictPlpDataSettings(
  studyStartDate = '20000101',
  studyEndDate = '20200101',
  firstExposureOnly = TRUE,
  washoutPeriod = 30
)
```

```
restrictPlpDataSettings <- PatientLevelPrediction::createRestrictPlpDataSettings(
  firstExposureOnly = TRUE,
  washoutPeriod = 30
)

plpData <- PatientLevelPrediction::getPlpData(
  databaseDetails = databaseDetails,
  covariateSettings = covariateSettings,
  restrictPlpDataSettings = restrictPlpDataSettings
)
```

```
##   |                                                                      |
```

```
## Warning: The 'oracleTempSchema' argument is deprecated. Use 'tempEmulationSchema' instead.
## This warning is displayed once every 8 hours.
```

```
## Constructing features on server
##   |                                                                      |
## Fetching data from server
## Fetching data took 0.184 secs
```

Defining a training set.

Most of the time we split the dataset into training and a test set. In order to prepare the data for fitting the model we have the function `MakeTraingSet`. What copies features of the function `patientLevelPrediction::runPlp`. In order to run it we have to create our settings: `populationSettings`, `executeSettings`, `splitSettings`, `sampleSettings`, `featureEngineeringSettings`, `preprocessSettings`. besides all these settings it also needs the plpData and the outcomeId.

```
populationSettings <- PatientLevelPrediction::createStudyPopulationSettings(
  binary = TRUE,
  includeAllOutcomes = FALSE,
  firstExposureOnly = FALSE,
  washoutPeriod = 180,
  removeSubjectsWithPriorOutcome = FALSE,
  priorOutcomeLookback = 99999,
  requireTimeAtRisk = TRUE,
  minTimeAtRisk = 1,
  riskWindowStart = 1,
  startAnchor = 'cohort start',
  riskWindowEnd = 7300,
  endAnchor = 'cohort start'
)
executeSettings <- PatientLevelPrediction::createExecuteSettings(
  runSplitData = TRUE,
  runSampleData = FALSE,
  runfeatureEngineering = FALSE,
  runPreprocessData = TRUE,
  runModelDevelopment = TRUE,
  runCovariateSummary = TRUE
)
splitSettings <- PatientLevelPrediction::createDefaultSplitSetting(
```

```
  testFraction = 0.25,
  trainFraction = 0.75,
  splitSeed = 123,
  nfold = 3,
  type = 'stratified'
)
sampleSettings <- PatientLevelPrediction::createSampleSettings(
  type = 'none'
)
featureEngineeringSettings <-
  PatientLevelPrediction::createFeatureEngineeringSettings(
  type = 'none'
)
preprocessSettings <- PatientLevelPrediction::createPreprocessSettings(
  minFraction = 0,
  normalize = TRUE,
  removeRedundancy = TRUE
)

TrainingSet <- PlasmodeSim::MakeTraingSet(
  plpData = plpData,
  executeSettings = executeSettings,
  populationSettings = populationSettings,
  splitSettings = splitSettings,
  sampleSettings = sampleSettings,
  preprocessSettings = preprocessSettings,
  featureEngineeringSettings = featureEngineeringSettings,
  outcomeId = 3
)
```

```
## Outcome is 0 or 1
## seed: 123
## Creating a 25% test and 75% train (into 3 folds) random stratified split by class
## Data split into 656 test cases and 1974 train cases (658, 658, 658)
## Train Set:
## Fold 1 658 patients with 120 outcomes - Fold 2 658 patients with 120 outcomes - Fold 3 658 patients w
## 103 covariates in train data
## Test Set:
## 656 patients with 119 outcomes
## Removing 2 redundant covariates
## Normalizing covariates
## Tidying covariates took 0.491 secs
## Train Set:
## Fold 1 658 patients with 120 outcomes - Fold 2 658 patients with 120 outcomes - Fold 3 658 patients w
## 101 covariates in train data
## Test Set:
## 656 patients with 119 outcomes
```

Fitting the model with censoring

We pick the desired model by setting the `modelsettings`. Then we can run the function `fitModelWithCensoring`. This function fits two plpModels one for the censoring and one for outcomes, both of the type specified in the modelsettings. It stores these plpModels in a list.

```
modelSettings <- PatientLevelPrediction::setCoxModel()

fitCensor <- PlasmodeSim::fitModelWithCensoring(
  Trainingset = TrainingSet$Train,
  modelSettings = modelSettings
)
```

```
## Running Cyclops
## Done.
## GLM fit status:  OK
## Creating variable importance data frame
## Prediction took 0.153 secs
## Running Cyclops
## Done.
## GLM fit status:  OK
## Creating variable importance data frame
## Prediction took 0.141 secs
```

Generating new outcomes times

Now that we have our model with the censoring, we can simulate new data. We call the function `simulateSurvivaltimesWithCensoring`

```
NewOutcomes <- PlasmodeSim::simulateSurvivaltimesWithCensoring(
  censorModel = fitCensor,
  plpData = plpData,
  population = TrainingSet$Train$labels,
  populationSettings = populationSettings,
  numberToSimulate = 10
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.175 secs
## Prediction took 0.249 secs
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.167 secs
## Prediction took 0.256 secs
```

```
head(NewOutcomes)
```

```
##   rowId survivalTime outcomeCount
## 1   425         6096            0
## 2  1557         7293            0
## 3  2066         2024            0
## 4   664         1329            0
## 5    48         5593            0
## 6   299           18            1
```

Since the censoring model Stores to models as a list one can easily generate unsensored outcomes by doing:

```
newdata <- PlasmodeSim::simulateSurvivaltimes(
  plpModel = fitCensor$outcomesModel,
  plpData = plpData,
  numberToSimulate = 10,
  population = TrainingSet$Train$labels,
  populationSettings = populationSettings
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.174 secs
## Prediction took 0.254 secs
```

```
head(newdata)
```

```
##   rowId outcome
## 1  2536    7300
## 2  1882    7300
## 3  1494    7300
## 4  1609    7300
## 5   911    7300
## 6  2610    7300
```

Defining an unfitted model

Just as before we can define a model that has not been fitted to the data. We specify a cox model by specifying the coefficients/parameters and the baseline survival function.

```
plpModel <- fitCensor$outcomesModel
coeff <- plpModel$model$coefficients
survival <- plpModel$model$baselineSurvival$surv
times <- plpModel$model$baselineSurvival$time

unfittedmodel <- PlasmodeSim::defineCoxModel(
  coefficients = coeff,
  baselinehazard = survival,
  timesofbaselinhazard = times,
  featureEngineering = NULL #  = NULL is the standard setting.
)

newdata <- PlasmodeSim::simulateSurvivaltimes(
  plpModel = unfittedmodel,
  plpData = plpData,
  numberToSimulate = 10,
  population = TrainingSet$Train$labels,
  populationSettings = populationSettings
)
```

```
## Prediction took 0.172 secs
```

```
head(newdata)
```

```
##   rowId outcome
## 1    17      18
## 2  1783    7300
## 3  2600    7300
## 4   964    7300
## 5    30      81
## 6  1182    7300
```

Defining an unfitted model with censoring

There is no function to define an unfitted model with censoring. That is because this can be done easily by making to cox models and storing them in a list. This elements in this list should have the names `censorModel` and `outcomeModel`.

```
#we can swap outcomes with censoring.
unfittedcensor<- list(censorModel = unfittedmodel,
                      outcomesModel = fitCensor$outcomesModel)

NewOutcomes <- PlasmodeSim::simulateSurvivaltimesWithCensoring(
  censorModel = unfittedcensor,
  plpData = plpData,
  population =  TrainingSet$Train$labels,
  populationSettings = populationSettings,
  numberToSimulate = 200
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.17 secs
## Prediction took 0.249 secs
## Prediction took 0.181 secs
```

```
head(NewOutcomes)
```

```
##   rowId survivalTime outcomeCount
## 1  1393           71            0
## 2  1363           36            0
## 3   485         7300            0
## 4   769         7300            0
## 5   244           30            0
## 6   614         7300            0
```

Adjusting the BaselineSurvival

If one want to get a grip on the outcome count on a specific time one can call the function `adjustBaselineSurvival`. This changes the base line function of a model such that, for the training data at the specified time the outcome rate is a specified probability. Since this function solves an equation it needs an specified interval to find this solution.

```
adjustedModel <- PlasmodeSim::adjustBaselineSurvival(
  plpModel = plpModel,
  TrainingSet = TrainingSet$Train,
  plpData = plpData,
  populationSettings = populationSettings,
  timeToFixAt = 3592,
  propToFixWith = 0.87,
  intervalSolution= c(-100,100)
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.18 secs
## Prediction took 0.248 secs
```

```
NewOutcomes <- PlasmodeSim::simulateSurvivaltimesWithCensoring(
  censorModel = list(censorModel = fitCensor$outcomesModel,
                     outcomesModel = adjustedModel),
  plpData = plpData,
  population =  TrainingSet$Train$labels,
  populationSettings = populationSettings,
  numberToSimulate = 2000
)
```

```
## Prediction took 0.18 secs
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.179 secs
## Prediction took 0.247 secs
```

```
head(NewOutcomes)
```

```
##   rowId survivalTime outcomeCount
## 1  2367           13            1
## 2   404           33            1
## 3  1501           14            1
## 4  1545           19            1
## 5  1942            0            1
## 6  1862           18            1
```

Plotting Kaplan Meier estimates

The function `kaplanMeierPlot` visualised the kamplanmeier estimate of a given dataset. It works with ggplot. We can easily compare the simulated data sets with the real dataset by putting them in one plot. For the true data set we set the colour to red.

```
NewOutcomes <- PlasmodeSim::simulateSurvivaltimesWithCensoring(
  censorModel = fitCensor,
  plpData = plpData,
  population = TrainingSet$Train$labels,
  populationSettings = populationSettings,
  numberToSimulate = 1974
)
```

```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.181 secs
## Prediction took 0.247 secs
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.188 secs
## Prediction took 0.25 secs
```

```
NewOutcomes2 <- PlasmodeSim::simulateSurvivaltimesWithCensoring(
  censorModel = fitCensor,
  plpData = plpData,
  population = TrainingSet$Train$labels,
  populationSettings = populationSettings,
  numberToSimulate = 1974
)
```

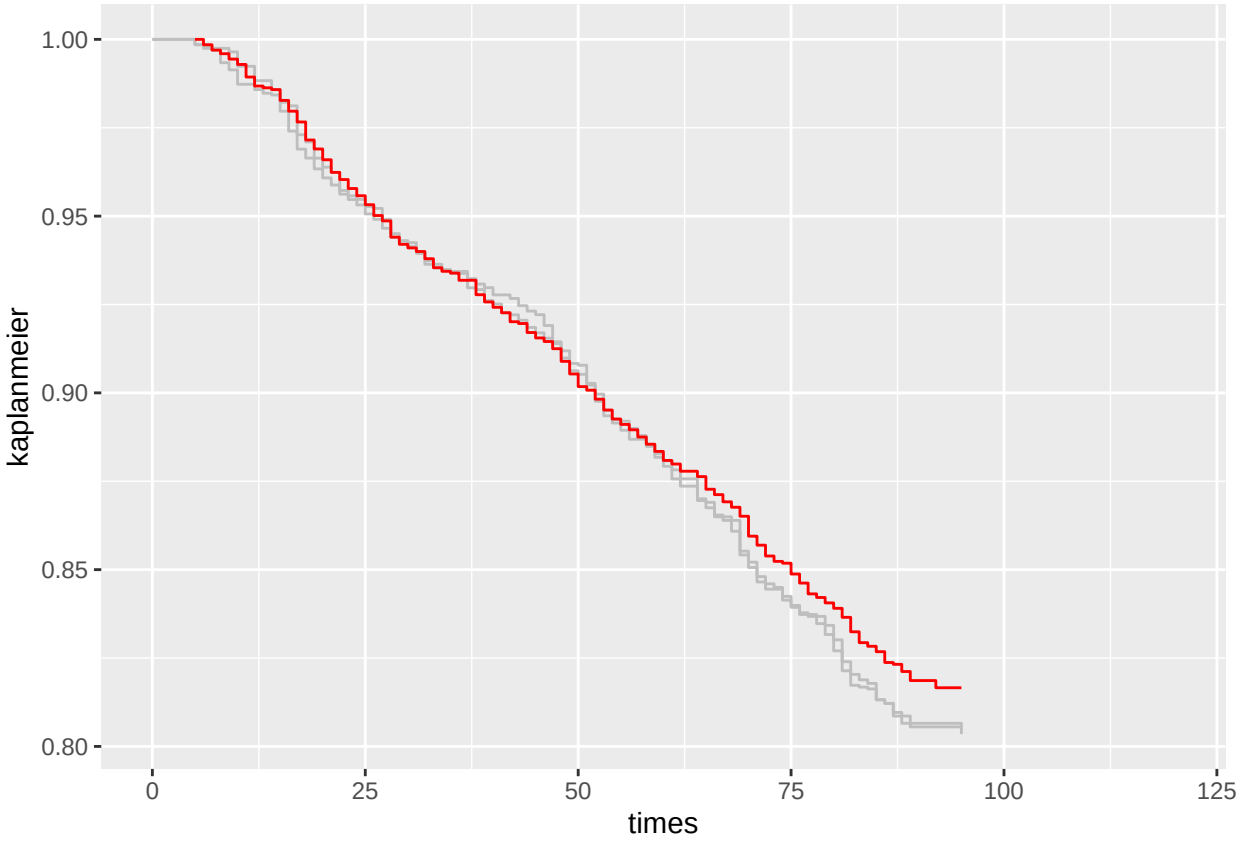
```
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.177 secs
## Prediction took 0.252 secs
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.175 secs
## Prediction took 0.255 secs
```

```
ggplot2::ggplot()+
  PlasmodeSim::KaplanMeierPlot( NewOutcomes )+
  PlasmodeSim::KaplanMeierPlot( NewOutcomes2 )+
  PlasmodeSim::KaplanMeierPlot( TrainingSet$Train$labels, colour = 'red' )+
  ggplot2::xlim(c(0,120))
```

```
## Warning: Removed 499 rows containing missing values (‘geom_step()‘).
```

```
## Warning: Removed 497 rows containing missing values (‘geom_step()‘).
```

```
## Warning: Removed 790 rows containing missing values (‘geom_step()‘).
```



runPlasmode

the function runPlasmode returns some new simulated survivaltimes, from a model it fits.

```
runPlas <- PlasmodeSim::runPlasmode(
  plpData = plpData,
  outcomeId = 3,
  populationSettings = populationSettings,
  splitSettings = splitSettings,
  sampleSettings = sampleSettings,
  featureEngineeringSettings = featureEngineeringSettings,
  preprocessSettings = preprocessSettings,
  modelSettings = modelSettings,
  executeSettings = executeSettings,
  numberToSimulate = 5
)
```

```
## Outcome is 0 or 1
## seed: 123
## Creating a 25% test and 75% train (into 3 folds) random stratified split by class
## Data split into 656 test cases and 1974 train cases (658, 658, 658)
## Train Set:
## Fold 1 658 patients with 120 outcomes - Fold 2 658 patients with 120 outcomes - Fold 3 658 patients w
## 103 covariates in train data
## Test Set:
```

```
## 656 patients with 119 outcomes
## Removing 2 redundant covariates
## Normalizing covariates
## Tidying covariates took 0.496 secs
## Train Set:
## Fold 1 658 patients with 120 outcomes - Fold 2 658 patients with 120 outcomes - Fold 3 658 patients w
## 101 covariates in train data
## Test Set:
## 656 patients with 119 outcomes
## Running Cyclops
## Done.
## GLM fit status:  OK
## Creating variable importance data frame
## Prediction took 0.145 secs
## Running Cyclops
## Done.
## GLM fit status:  OK
## Creating variable importance data frame
## Prediction took 0.134 secs
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.178 secs
## Prediction took 0.248 secs
## Removing infrequent and redundant covariates and normalizing
## Removing infrequent and redundant covariates covariates and normalizing took 0.17 secs
## Prediction took 0.249 secs
```

```
runPlas
```

```
##   rowId survivalTime outcomeCount
## 1   572         5484            0
## 2  1726         6611            0
## 3   419         7111            0
## 4   522           27            1
## 5   425         7293            0
```

Possible extencions

Here is a list of future extensions to make the package more useful:

- The runPlasmode should have a working analysisId, analysisName and logsettings, like runPlp has.
- one could extend the fitmodel by adding an option for a Differen models for the censoring.
- Take a look at the feature ingeneering in the `definecoxmodel` function.
- Add more functions that define unfitted models.

- Make it faster by filtering the population on the row ids drawn, before making their outcomes.