Using glmnetr

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The Package

For some datasets, for example when there are collinearities in the design matrix x, glmnet may have very long run times when fitting the relaxed lasso model, making it difficult to get solutions either from cv.glmnet or even glmnet. In this package, glmnetr, we provide a workaround and solve for the unpenalized relaxed model where gamma=0 for the linear, logsite and Cox regression model structures using the stats glm() function and the R survival package coxph() function. If you are not fitting relaxed lasso models, or if you are able to reasonably quickly get convergence using glmnet, then this package may not be of much benefit to you. Note, while this package may allow one to fit relaxed lasso models that have difficulties converging using glmnet, this package does not afford the full function and versatility of glmnet.

In addition to fitting the relaxed lasso model this package also includes the function cv.glmnetr() to perform a cross validation (CV) to identify hyperparameters for a lasso fit, much like the cv.glmnet() function of the glmnet package. Additionally, the package includes the function nested.glmnetr() to perform a nested CV to assess the fit of a cross validation informed lasso model fit. If though you are fitting not a relaxed lasso model but an elastic-net model, then the R-packages nestedcv (https://cran.r-project.org/package=nestedcv), 'glmnetSE' (https://cran.r-project.org/package=glmnetSE) or others may provide greater functionality when performing a nested CV.

As with the *glmnet* package, this package passes most relevant information to the output object which can be evaluated using plot, summary and predict functions. Use of the *glmnetr* package has many similarities to the *glmnet* package and it is recommended that the user of *glmnetr* first become familiar with the *glmnet* package (https://cran.r-project.org/package=glmnet), with the "An Introduction to glmnet" and "The Relaxed Lasso" being especially helpful in this regard.

Data requirements

The basic data elements for input to the *glmnetr* analysis programs are similar to those of *glmnet* and include 1) a matrix of predictors and 2) an outcome variable or variables in vector form. For the estimation of the "fully" relaxed models (where gamma=0) the package is set up to fit the "gaussian" and "binomial" models using the *stats* glm() function and Cox survival models using the the coxph() function of the *survival* pacakge. When fitting the Cox model the outcome model variable is interpreted as the "time" variable in the Cox model, and one must also specify 3) a variable for event, agian in vector form, and optionally 4) a variable for start time, also in vector form. Row i of the predictor matrix and element i of the outcome vector(s) are to include the data for the same sampling unit.

An example dataset

To demonstrate usage of glmnetr we first generate a data set for analysis, run an analysis and evaluate using the plot(), summary() and predict() functions.

The code

```
# Simulate data for use in an example relaxed lasso fit of survival data
# first, optionally, assign a seed for random number generation to get applicable results
set.seed(116291949)
simdata=glmnetr.simdata(nrows=1000, ncols=100, beta=NULL)
```

generates simulated data for analysis. We extract data in the format required for input to the *glmnetr* programs.

```
# Extract simulated survival data
xs = simdata$xs  # matrix of predictors
y_ = simdata$yt  # vector of survival times
event = simdata$event  # indicator of event vs. censoring
```

Inspecting the predictor matrix we see

```
# Check the sample size and number of predictors
print(dim(xs))

## [1] 1000 100

# Check the rank of the design matrix, i.e. the degrees of freedom in the predictors
rankMatrix(xs)[[1]]
## [1] 94
```

```
# Inspect the first few rows and some select columns
print(xs[1:10,c(1:12,18:20)])
```

```
X1 X2 X3 X4 X5 X6 X7 X8 X9 X10 X11 X12
                                                        X18
                                                                   X19
                               0
                                  0
                                               1 0.1513225 -0.4034383
##
    [1,]
                      0
                         0
                            0
                                           0
                                                                        0.35250844
##
    [2,]
         1
             0
                0
                   0
                      1
                         0
                            0
                               1
                                  0
                                       0
                                           0
                                               0 -1.1610480
                                                             0.5533030
                                                                        0.14578868
   [3,]
                   1
                      0
                         0
                            1
                                               0 -0.3292269
                                                             0.3086399 -0.48443836
   [4,]
                   0
                      0
                         0
                            0
                               0 0
                                               0 2.0635214 -0.5500741 -0.02173104
          1
             1
                0
                                      1
                                           0
##
    [5,]
          1
             0
                0
                   0
                      1
                         0
                            0
                               1
                                  0
                                      0
                                           0
                                               0 0.3905722 -0.6836452 -0.37643201
                      0
                         0
                            0
                               0
##
   [6,]
         1
             0
                1
                   0
                                 1
                                      0
                                           0
                                               0 -0.2397597
                                                            1.6909447 0.49599945
   [7,]
          1
             0
                   0
                      0
                         0
                            0
                              1 0
                                           0
                                               0 -0.5592424  0.2314638 -0.53198341
   [8,]
                      0
                         0
                            0
                               0 0
          1
             0
                0
                   1
                                       0
                                          1
                                               0 -1.0050514 0.5319574 0.54287646
   [9,]
          1
             0
                0
                   1
                      0
                         0
                            0
                               0 0
                                       0
                                           1
                                               0 1.2548034 0.8213164
                                                                        0.17067691
                                               0 -0.3079151 -0.6105910 -0.88711869
## [10,]
          1
             0
                0
                   0
                      1
                         0
                            0
                               0
                                           0
```

Cross validation (CV) informed relaxed lasso model fit

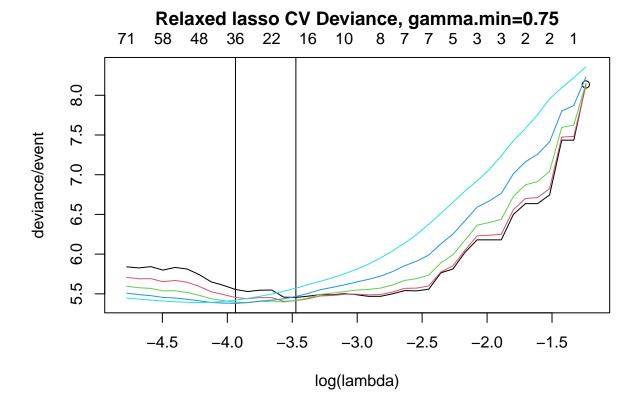
To fit a relaxed lasso model and get reasonable hyperparameters for lambda and gamma, and summarize the cross-validated "tuned" model fit, we can use the function cv.glmnet() and summary() functions.

```
# Fit a relaxed lasso model informed by cross validation
cv.cox.fit = suppressWarnings( cv.glmnetr(xs, NULL, y_, event, family="cox", track=0) )
```

Note, in the derivation of the relaxed lasso model fits, individual coefficients may be unstable even when the model may be stable which elicits warning messages. Thus we "wrapped" the call to cv.glmnetr() within the suppressWarnings() function to suppress excessive warning messages in this vignette. The first term in the call to cv.glmnetr(), xs, is the design matrix for predictors. The second input term, here NULL, is for the start time in case (start, stop) time data setup is used in a Cox survival model. The third term is the outcome variable for the linear regression or logistic regression model and the time of event or censoring in case of the Cox model, and finally the forth term is the event indicator variable for the Cox model taking the value 1 in case of an event or 0 in case of censoring at time y_. The forth term would be NULL for either linear or logistic regression. Currently the options for family are "guassian" for linear regression, "binomial" for logistic regression (both using the stats glm() function) and "cox" for the Cox proportional hazards regression model using the coxph() function of the R survival package. If one sets track=1 the program will update progres in the R console, else for track=0 it will not. | Before numerically summarizing the model fit, or inspecting the coefficient estimates, we plot the average deviances using the plot function.

Plot cross validation average deviances for a relaxed lasso model plot(cv.cox.fit)

```
## min CV average deviance (max log likelihood) for
## relaxed at log(lambda) = -3.937, gamma.min = 0.75, df = 36
## fully relaxed at log(lambda) = -3.472, df = 18
## fully penalized at log(lambda) = -4.216, df = 48
```



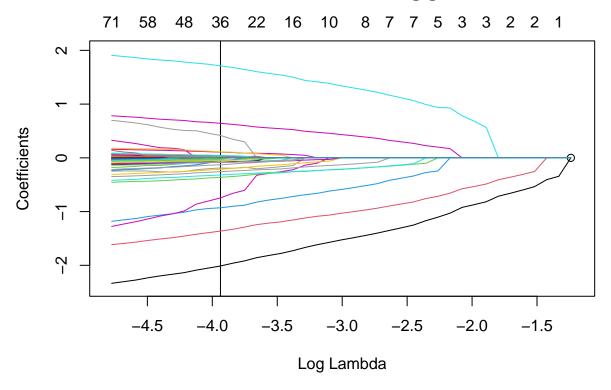
In that to maximize the log-likelihoods is to minimize deviance we inspect these curves for a minimum. The minimizing lambda is indicated by the left most vertical line, here about log(lambda) = -3.94. The minimizing gamma is 0.75 and described in the title. Whereas there is no legend here for gamma, when non-zero coefficients start to enter the model as the penalty is reduced, here shown to the right, deviances

will tend to be smaller for gamma = 0, greater for gamma = 1 and in between for other gammas values. From this figure we also see that at lambda=0.75 the deviance is hardly distinguishable for gamma ranging from 0.5 to 1. More relevant we see that the fully relaxed lasso (gamma=0) and indicated by the right most vertical line, achieves a "nearly" minimal deviance at about -3.47.

```
# Plot coefficients informed by a cross validation
plot(cv.cox.fit, coefs=TRUE)
```

```
## min CV average deviance (max log likelihood) ## at log(lambda.min) = -3.937, gamma.min = 0.75, df = 36
```

Relaxed lasso fit at minimizing gamma 0.75

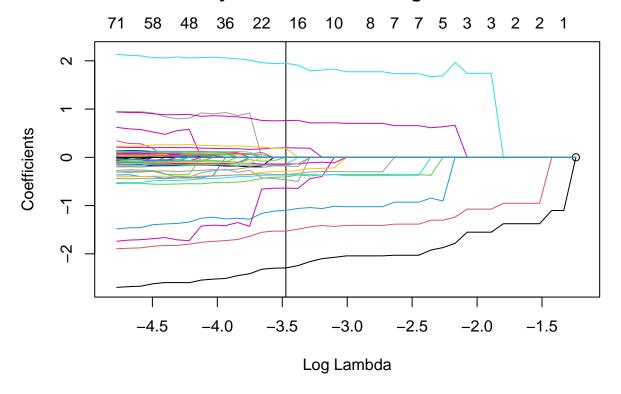


In this plot of coefficients we use the same orientation for lambda as in the plot for deviances with larger values of the lambda penalty to the right and corresponding to fewer non-zero coefficients. The displayed coefficients are for the minimizing gamma=0.75 as noted in the tile, and the minimizing lambda indicated by the vertical line. Now, since the fully relaxed lasso model had a deviance almost that of the relaxed lasso model we also plot the coefficients using the option gam=0.

```
# Plot fully relaxed coefficients informed by a cross validation
plot(cv.cox.fit, coefs=TRUE, gam=0)
```

```
## Fully relaxed min CV average deviance (max log likelihood) ## at log(lambda.min) = -3.472, df = 18
```

Fully relaxed lasso fit for gamma = 0



In addition to simply showing how the coefficients change as the lambda penalty is decreased, this plot shows how the coefficients change for the un-penalized (fully relaxed) model with gamma=0 as lambda decreases. In particular we see the coefficients become slightly larger in magnitude as the lambda penalty decreases and also as additional terms come into the model. This is not unexpected as omitted terms from the Cox model tend to bias coefficients toward 0 more than increase the standard error. We also see, as too indicated in the deviance plot, the number of model non-zero coefficients, 18, to be substantially less than the 36 from the relaxed lasso fit and the 48 from the fully penalized lasso fit.

| The summary function describes the relaxed lasso fit informed by CV.

```
# Summarize relaxed lasso model fit informed by cross validation summary(cv.cox.fit)
```

```
##
##
     The relaxed minimum is obtained for lambda = 0.01950023, index = 30 and gamma = 0.75
##
     with df (number of non-zero terms) = 36, average deviance = 5.380322 and beta =
              X4
                             Х5
                                            X8
##
                                                          X14
                                                                         X15
##
   -9.298178e-01
                   1.711721e+00 -1.885456e-01 -7.454261e-01
                                                               1.190965e-14
##
             X16
                            X17
                                           X18
                                                          X19
                                                                         X20
    4.167433e-01
                  -1.302087e-15
                                 -1.362967e+00
                                                -3.625131e-01
                                                                2.922682e-02
##
##
             X21
                            X22
                                           X23
                                                          X24
                                                                         X25
##
   -3.182677e-01
                   6.426824e-01
                                 -2.134638e-01
                                                -2.569618e-01
                                                              -2.012441e+00
##
             X29
                            X30
                                           X34
                                                          X35
                                                                         X38
                   2.816325e-02
##
    2.389336e-02
                                  2.602897e-02
                                                 2.119959e-02
                                                                1.064479e-01
             X39
                                           X49
                                                          X50
                                                                         X58
##
                            X43
##
    2.293174e-02 -5.218288e-02 -7.819052e-02
                                                3.211853e-02
                                                               3.392804e-02
             X59
                            X60
                                           X61
                                                          X62
                                                                         X67
##
   -3.948692e-02 -4.923017e-02 -7.808802e-02 -8.469542e-02
                                                               1.799604e-02
```

```
##
             X71
                           X72
                                          X77
                                                        X87
                                                                       X96
   -4.703098e-02 -1.302645e-01 4.472362e-02 1.123160e-01 -8.482900e-02
##
##
             X99
   -2.308179e-02
##
##
##
     The fully relaxed (gamma=0) minimum is obtained for lambda = 0.03104988 and index = 25
##
     with df (number of non-zero terms) = 17, average deviance = 5.455056 and beta =
##
           Х4
                      Х5
                                  Х8
                                            X14
                                                       X18
                                                                   X19
##
   -1.0991234
               1.9492327 -0.4643855 -0.6377441 -1.5308945 -0.4075762 -0.3687472
##
          X22
                     X23
                                 X24
                                            X25
                                                       X38
                                                                   X61
                                                                              X62
##
    0.7625238
              -0.2999622
                         -0.3593211
                                     -2.2920690
                                                 0.1993155 -0.1477441 -0.1403819
          X72
                     X87
                                 X96
##
##
   -0.1784984
               0.1874497 -0.1588458
##
##
     The UNrelaxed (gamma=1) minimum is obtained for lambda = 0.01475121 and index = 33
##
     with df (number of non-zero terms) = 48, average deviance = 5.390245
##
##
##
     Order coefficients entered into the lasso model (1st to last):
##
    [1] "X25" "X18" "X5"
                          "X22" "X4"
                                      "X19" "X21" "X24" "X23" "X62" "X14" "X38"
##
   [13] "X8" "X72" "X96" "X61" "X87" "X59" "X35" "X49" "X50" "X16" "X34" "X71"
   [25] "X77" "X30" "X39" "X43" "X58" "X60" "X20" "X29" "X67" "X99" "X12" "X28"
   [37] "X84" "X98" "X51" "X55" "X88" "X6" "X11" "X33" "X78" "X40" "X66" "X68"
```

In the summary output we first see the relaxed lasso model fit based upon the (lambda, gamma) pair which minimizes the cross validated average deviance. Next is the model fit based upon the lambda that minimizes the cross validated average deviance along the path where gamma=0, that is among the fully relaxed lasso models. After that is information on the fully penalized lasso fit, but without the actual coefficient estimates. These estimates can be printed using the option printg1=TRUE, but are suppressed by default for space. Finally, the order that coefficients enter the lasso model as the penalty is decreased is provided, which gives some indication of relative model importance of the coefficients. Because, though, the differences in successive lambda values used in the numerical algorithms may allow multiple new terms to enter into the model between successive numerical steps, the ordering in this list may not be strict. If the user would want they could read lambda from output\$lambda, set up a new lambda with finer steps and rerun the model. Our experience though is that this does not generally lead to a meaningfully different model and so is not done by default or as option. One can as well use the predict function to get the coefficients for the lasso model, or the xs new*beta for a new design matrix xs new. In contrast to the summary function which simply displays coefficients, the predict function provides an outpout object in vector form (or a list with two vectors) and so can more easily be used for further calculations. By default the summary function will use the (lambda, gamma) pair that minimizes the average CV deviances. One can also specify lam=NULL and gam=1 to use the fully penalized lasso best fit, that use the solution that minimizes the CV deviance with respect to lambda while holding gamma=1, or gam=0 to use the fully relaxed lasso best fit, that is minimizes while holding gamma=0. One can also numerically specify both lam for lambda and gam for gamma. Within the package lambda and gamma usually denote vectors for the search algorithm and so other names are used uere.

```
# Get coefficients
beta = predict(cv.cox.fit)
```

```
##
## (lambda, gamma) pair minimizing CV average deviance is used
```

Print out the non-zero coefficients

beta\$beta

```
Х5
                                           Х8
                                                         X14
                                                                       X15
                                                             1.190965e-14
##
   -9.298178e-01
                  1.711721e+00 -1.885456e-01 -7.454261e-01
##
             X16
                           X17
                                          X18
                                                        X19
##
    4.167433e-01 -1.302087e-15 -1.362967e+00 -3.625131e-01
                                                              2.922682e-02
##
             X21
                           X22
                                          X23
                                                        X24
   -3.182677e-01
                  6.426824e-01 -2.134638e-01 -2.569618e-01 -2.012441e+00
##
##
             X29
                           X30
                                          X34
                                                         X35
    2.389336e-02
                  2.816325e-02 2.602897e-02
                                              2.119959e-02
                                                             1.064479e-01
##
##
             X39
                           X43
                                          X49
                                                        X50
##
    2.293174e-02 -5.218288e-02 -7.819052e-02
                                               3.211853e-02
                                                              3.392804e-02
                           X60
##
             X59
                                          X61
                                                        X62
   -3.948692e-02 -4.923017e-02 -7.808802e-02 -8.469542e-02
                                                         X87
##
             X71
                           X72
                                          X77
   -4.703098e-02 -1.302645e-01 4.472362e-02 1.123160e-01 -8.482900e-02
##
             X99
## -2.308179e-02
```

Print out all coefficients

beta\$beta

```
Х5
##
              X1
                             X2
                                           ХЗ
                                                          Х4
    0.000000e+00
                  0.000000e+00 0.000000e+00 -9.298178e-01
##
##
              Х6
                             Х7
                                           Х8
                                                          χ9
                  0.000000e+00 -1.885456e-01 0.000000e+00
##
    0.00000e+00
                                                               0.000000e+00
##
             X11
                            X12
                                          X13
                                                         X14
                                                                        X15
##
    0.00000e+00
                  0.00000e+00
                                0.000000e+00 -7.454261e-01
                                                               1.190965e-14
             X16
                            X17
                                           X18
                                                                        X20
##
                                                         X19
    4.167433e-01 -1.302087e-15 -1.362967e+00 -3.625131e-01
##
                                                               2.922682e-02
##
             X21
                            X22
                                           X23
                                                         X24
   -3.182677e-01
                  6.426824e-01 -2.134638e-01 -2.569618e-01 -2.012441e+00
##
             X26
                            X27
                                           X28
                                                         X29
##
##
    0.000000e+00
                  0.000000e+00
                                 0.000000e+00
                                                2.389336e-02
                                                               2.816325e-02
##
             X31
                            X32
                                           X33
                                                         X34
                                                                        X35
    0.000000e+00
                  0.000000e+00
                                 0.000000e+00
##
                                                2.602897e-02
                                                               2.119959e-02
##
             X36
                            X37
                                           X38
                                                         X39
##
    0.000000e+00
                  0.000000e+00
                                 1.064479e-01
                                                2.293174e-02
                                                               0.000000e+00
##
             X41
                            X42
                                           X43
                                                         X44
##
    0.00000e+00
                  0.000000e+00 -5.218288e-02
                                                0.000000e+00
                                                               0.000000e+00
##
             X46
                                           X48
##
    0.000000e+00
                  0.000000e+00
                                 0.000000e+00 -7.819052e-02
                                                               3.211853e-02
##
             X51
                            X52
                                           X53
                                                         X54
    0.000000e+00
                  0.000000e+00
                                 0.000000e+00
                                                0.000000e+00
                                                               0.000000e+00
##
##
             X56
                            X57
                                           X58
                                                         X59
    0.000000e+00
                  0.000000e+00
                                 3.392804e-02 -3.948692e-02
##
                                                              -4.923017e-02
                                           X63
##
             X61
                                 0.000000e+00
##
   -7.808802e-02 -8.469542e-02
                                                0.000000e+00
                                                               0.000000e+00
             X66
                                           X68
##
                            X67
##
    0.000000e+00
                  1.799604e-02
                                 0.00000e+00
                                                0.000000e+00
                                                               0.000000e+00
                                          X73
                            X72
                                                         X74
  -4.703098e-02 -1.302645e-01 0.000000e+00 0.000000e+00 0.000000e+00
```

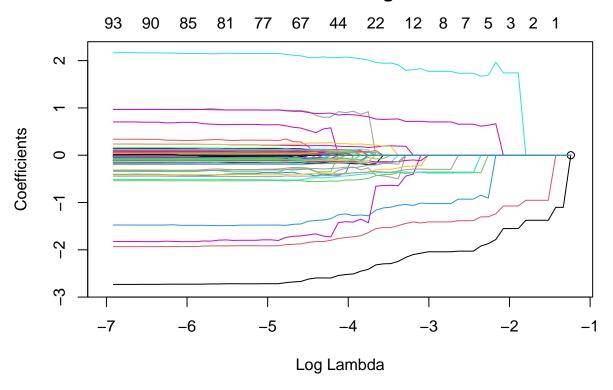
```
##
             X76
                            X77
                                          X78
                                                         X79
                                                                        X80
                                               0.000000e+00
    0.000000e+00
                  4.472362e-02
                                 0.000000e+00
                                                              0.000000e+00
##
##
             X81
                            X82
                                          X83
                                                         X84
                                                                        X85
    0.000000e+00
                  0.00000e+00
                                 0.00000e+00
                                                0.000000e+00
                                                              0.00000e+00
##
##
             X86
                            X87
                                          X88
                                                         X89
                                                                        X90
    0.000000e+00
##
                   1.123160e-01
                                 0.000000e+00
                                                0.00000e+00
                                                              0.000000e+00
##
             X91
                            X92
                                          X93
                                                         X94
                                                                        X95
##
    0.000000e+00
                  0.000000e+00
                                 0.000000e+00
                                               0.000000e+00
                                                              0.000000e+00
##
             X96
                            X97
                                          X98
                                                         X99
                                                                       X100
                  0.000000e+00
                                 0.000000e+00 -2.308179e-02
   -8.482900e-02
                                                              0.000000e+00
# Get the predicteds (linear predictors) for the original data set
predicteds = predict(cv.cox.fit, xs)
##
##
    (lambda, gamma) pair minimizing CV average deviance is used
# Print out the first few predicteds
predicteds[1:20]
##
    [1]
         0.1009869 4.3123200 -4.4673094 -1.7814957 0.9077405 -1.0938730
    [7]
         4.6147550 -0.1989544 -6.0377112 -1.6112803 -0.8198837 2.1165700
   [13] -1.1446918 -2.1868484
                               1.7288336 -0.1977422 -1.0923555 -4.4471458
  [19]
         2.2903899 -2.8503090
```

Model fit without cross validation

We can as well fit a relaxed lasso model without doing a CV. For this case one can still plot the coefficients but when the minimizing lambda and gamma are not informed by CV one is to specify which gamma should be used for the plots. By default gamma=1, i.e. for the fully penalized lasso model, is used for the plots. One can plot the coefficient estimates for different gamma values, but these will usually be more meaningful when informed by the CV "tuned" hyperparameters values for lambda and gamma. One can also use the predict() function, again to output either coefficients or predicteds, i.e. xs_new*beta for a new design matrix xs_new. Such predicteds are often, for example in coxph(), included in the analysis output object under the name linear.predictors.

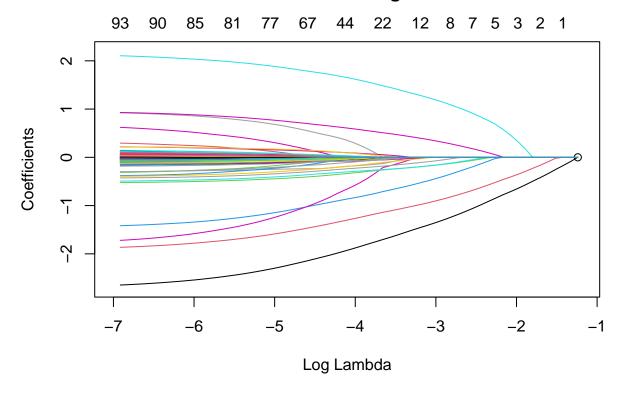
```
# Fit a model without cross validation
cox.fit = suppressWarnings( glmnetr(xs, NULL, y_, event, family="cox") )
# Plot coefficients of the fully relaxed lasso model
plot(cox.fit, gam=0)
```

Relaxed lasso fit for gamma = 0



Plot coefficients of the fully penalized lasso model
plot(cox.fit, gam=1)

Relaxed lasso fit for gamma = 1



```
# Get an arbitrary set of coefficients for this example
lam = cox.fit$lambda[min(20,length(cox.fit$lambda))]
predict(cox.fit,lam=lam,gam=1)$beta
##
           Х4
                      Х5
                                X18
                                            X19
                                                       X21
                                                                  X22
                                                                              X24
## -0.4445542
               1.1931259 -0.9052081 -0.1634296 -0.1607677 0.3425005 -0.0734942
##
          X25
## -1.3556991
```

Nested cross validation

Because the values for lambda and gamma informed by CV are specifically chosen to give a best fit, model fit statistics for the CV derived model will be biased. To address this one can perform a CV on the CV derived estimates, that is a nested cross validation as argued for in SRDM (Simon R, Radmacher MD, Dobbin K, McShane LM. Pitfalls in the Use of DNA Microarray Data for Diagnostic and Prognostic Classification. J Natl Cancer Inst (2003) 95 (1): 14-18. https://academic.oup.com/jnci/article/95/1/14/2520188). This is done here by the nested.glmnetr() function.

```
# A nested cross validation to evaluate a cross validation informed lasso model fit
# nested.cox.fit = nested.glmnetr(xs,NULL,y_,event,family="cox",track=1)
nested.cox.fit = suppressWarnings(nested.glmnetr(xs,NULL,y_,event,family="cox",track=0))
summary(nested.cox.fit)
```

```
Sample information including number of records, events, number of columns in
    design (predictor, X) matrix, and df (rank) of design matrix:
##
                             nevents xs.columns
##
       family
                        n
                   "1000"
                                "337"
                                           "100"
                                                        "94"
##
        "cox"
##
##
    Tuning parameters for lasso/rpart model:
##
       folds n
                       seed
          "10" "325180121"
##
##
##
    Nested Cross Validation averages for LASSO (1se and min), Relaxed LASSO, and gamma=0 LASSO:
##
##
         deviance per event
##
     lasso.1se
                  lasso.min
                             lasso.1seR
                                          lasso.minR lasso.1seRO lasso.minRO
        5.3569
                     5.2830
##
                                 5.3446
                                              5.3103
                                                           5.3808
                                                                        5.3726
##
##
         number of nonzero model terms :
##
     lasso.1se
                  lasso.min
                             lasso.1seR
                                          lasso.minR lasso.1seRO lasso.minRO
##
          26.1
                       50.7
                                    21.9
                                                36.7
                                                              7.0
                                                                          11.7
##
##
         linear calibration coefficient :
##
     lasso.1se
                  lasso.min
                             lasso.1seR
                                          lasso.minR lasso.1seRO lasso.minRO
##
        1.3028
                     1.0918
                                 1.2588
                                              1.0469
                                                           1.0898
                                                                        0.9771
##
         agreement (concordance):
##
##
     lasso.1se
                  lasso.min
                             lasso.1seR
                                          lasso.minR lasso.1seR0 lasso.minR0
##
        0.9193
                     0.9206
                                 0.9194
                                              0.9198
                                                           0.9137
                                                                        0.9143
##
##
    Naive agreement for cross validation informed lasso model :
##
     lasso.1se
                  lasso.min
                             lasso.1seR
                                         lasso.minR lasso.1seRO lasso.minRO
##
        0.9253
                     0.9315
                                  0.9253
                                              0.9313
                                                           0.9288
                                                                        0.9343
```

#names(nested.cox.fit)

Before providing analysis results the output first reports sample size and since this is for a Cox regression, the number of events, followed by the number of predictors and the df (degrees of freedom) of the design matrix, as well as some information on "Tuning parameters" which reflect the earlier work to compare the lasso model with stepwise procedures as described in JWHT (James, Witten, Hastie and Tibshirani, An Introduction to Statistical Learning with applications in R, 2nd ed., Springer, New York, 2021). In general we have found in practice that the lasso does better and so we do not present results here. (The tuned stepwise fits also take a long to run, part of the earlier motivation for the lasso model development.)

Next are the nested cross validation results. First are the per record (or per event in case of the Cox model) log-likelihoods which reflect the amount of information in each observation. Since we are not using large sample theory to base inferences we feel the per record are more intuitive, and they allow comparisons between datasets with unequal sample sizes. Next are the average number of model terms which reflect the complexity of the different models, even if in a naive sense, followed by the agreement statistics, here concordance, These nested cross validated concordances should be essentially unbiased for the given design, unlike the naive concordances where the same data are used to derive the model and calculate the concordances (see SRDM).

In addition to evaluating the CV informed relaxed lasso model using another layer of CV, the nested.glmnetr() function also runs cv.glmnetr() based upon the whole data set. Here we see, not unexpectedly, that the concordances estimated from the nested CV are slightly smaller than the concordances naively calculated using the original dataset. Depending on the data the nested CV and naive agreement measures, here concordance, can be very similar or disparate.

Following JWHT we provide information on the minimizing lasso models as well as the "1SE" models,

which are near to the minimizing lasso model fits, but of simpler nature. We though focus on the minimizing lasso fits recognizing that relaxed lasso and fully relaxed lasso fits generally provide models of simpler form while still optimizing a fit.

A summary for the CV fit can be produced by using the summary() function directly on a nested.glmnetr() output using the option cvfit=TRUE. Else one can also extract the CV fit by extracting the object\$cv.glmnet.fit, where object is the output object obtained when running nested.glmnetr(). The plot() and predict() functions can be applied directly to a nested.glmnetr() object without the cvfit option for futher evaluation or calculations for the CV model fit.

```
# Summary of the CV fit from a nested CV output
summary(nested.cox.fit, cvfit=TRUE)
```

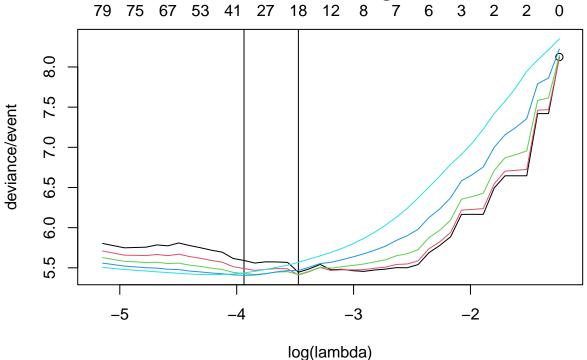
```
##
     The relaxed minimum is obtained for lambda = 0.01950023, index = 30 and gamma = 0.75
##
##
     with df (number of non-zero terms) = 36, average deviance = 5.407983 and beta =
##
              X4
                             Х5
                                            X8
                                                         X14
   -9.298178e-01
                   1.711721e+00
                                -1.885456e-01 -7.454261e-01
##
                                                               1.190965e-14
##
             X16
                            X17
                                           X18
                                                         X19
                                                                        X20
    4.167433e-01
                                -1.362967e+00
                                              -3.625131e-01
##
                  -1.302087e-15
                                                               2.922682e-02
##
             X21
                            X22
                                           X23
                                                         X24
                                                                        X25
##
   -3.182677e-01
                  6.426824e-01 -2.134638e-01 -2.569618e-01
                                                             -2.012441e+00
##
             X29
                            X30
                                           X34
                                                         X35
                                                                        X38
##
    2.389336e-02
                  2.816325e-02
                                 2.602897e-02
                                                2.119959e-02
                                                               1.064479e-01
##
             X39
                            X43
                                           X49
                                                         X50
                                                                        X58
##
    2.293174e-02
                  -5.218288e-02
                                -7.819052e-02
                                                3.211853e-02
                                                               3.392804e-02
##
             X59
                            X60
                                           X61
                                                         X62
                                                                        X67
##
   -3.948692e-02
                 -4.923017e-02
                                -7.808802e-02
                                               -8.469542e-02
                                                               1.799604e-02
##
             X71
                            X72
                                           X77
                                                         X87
                                                                        X96
   -4.703098e-02 -1.302645e-01 4.472362e-02 1.123160e-01 -8.482900e-02
##
##
             X99
   -2.308179e-02
##
##
##
     The fully relaxed (gamma=0) minimum is obtained for lambda = 0.03104988 and index = 25
     with df (number of non-zero terms) = 17, average deviance = 5.445049 and beta =
##
##
           Х4
                       Х5
                                  Х8
                                             X14
                                                        X18
                                                                    X19
                                                                               X21
   -1.0991234
               1.9492327 -0.4643855 -0.6377441 -1.5308945 -0.4075762 -0.3687472
##
##
          X22
                      X23
                                 X24
                                             X25
                                                        X38
                                                                    X61
                                                                               X62
              -0.2999622 -0.3593211 -2.2920690
                                                 0.1993155 -0.1477441 -0.1403819
##
    0.7625238
##
          X72
                     X87
                                 X96
##
   -0.1784984
               0.1874497 -0.1588458
##
##
     The UNrelaxed (gamma=1) minimum is obtained for lambda = 0.01475121 and index = 33
##
     with df (number of non-zero terms) = 48, average deviance = 5.415692
##
##
##
     Order coefficients entered into the lasso model (1st to last):
    [1] "X25" "X18" "X5"
                           "X22" "X4"
                                       "X19" "X21" "X24" "X23" "X62" "X14" "X38"
##
              "X72" "X96" "X61" "X87" "X59" "X35" "X49" "X50" "X16" "X34" "X71"
       "X77" "X30" "X39" "X43" "X58" "X60" "X20" "X29" "X67" "X99" "X12" "X28"
   [37] "X84" "X98" "X51" "X55" "X88" "X6" "X11" "X33" "X78" "X40" "X66" "X68"
```

Observe, the summary here is slightly different than obtained above running cv.glmnetr(). This is because the model is derived using a new call (instance) of the cv.glmnetr() function, and each CV uses by default a new random partitioning of the data.

Plot CV deviances from a nested CV output plot(nested.cox.fit)

```
## min CV average deviance (max log likelihood) for
## relaxed at log(lambda) = -3.937, gamma.min = 0.75, df = 36
## fully relaxed at log(lambda) = -3.472, df = 18
## fully penalized at log(lambda) = -4.216, df = 48
```

Relaxed lasso CV Deviance, gamma.min=0.75

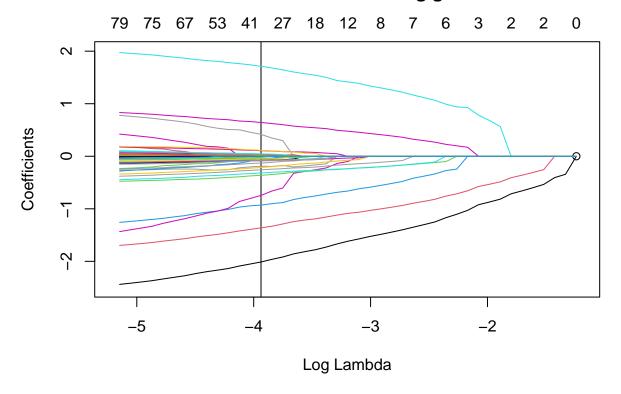


and

```
# Plot coefficients from a nested CV output
plot(nested.cox.fit, coefs=TRUE)
```

```
## min CV average deviance (max log likelihood)
## at log(lambda.min) = -3.937, gamma.min = 0.75, df = 36
```

Relaxed lasso fit at minimizing gamma 0.75



Summarizing, the summary() function with the cvfit=TRUE option as well as the plot() and predict() functions for a nested.glmnetr() object are then essentially the same as those for a cv.glmnetr() output object. The summary() function without the cvfit=TRUE option, though, regards the evaluation of the cv.glmnetr() fit and is different.

... or use the predict function on the CV fit embedded in the nested CV output predict(nested.cox.fit)\$beta

(lambda, gamma) pair minimizing CV average deviance is used ## ## Х4 Х5 Х8 X14 X15 -9.298178e-01 1.711721e+00 -1.885456e-01 -7.454261e-01 ## 1.190965e-14 ## X16 X17 X18 X19 X20 ## 4.167433e-01 -1.302087e-15 -1.362967e+00 -3.625131e-01 2.922682e-02 X21 X22 X23 X24 ## X25 ## -3.182677e-01 6.426824e-01 -2.134638e-01 -2.569618e-01 -2.012441e+00 ## X29 X30 X34 X35 X38 ## 2.389336e-02 2.816325e-02 2.602897e-02 2.119959e-02 1.064479e-01 ## X39 X43 X49 X50 X58 2.293174e-02 -5.218288e-02 -7.819052e-02 ## 3.211853e-02 3.392804e-02 ## X59 X60 X61 X62 -3.948692e-02 -4.923017e-02 -7.808802e-02 -8.469542e-02 ## 1.799604e-02 ## X77 X87 X96 -4.703098e-02 -1.302645e-01 4.472362e-02 1.123160e-01 -8.482900e-02 ## -2.308179e-02

Again, the plots and summary outputs from the nested.glmnetr() output are sightly different from what we saw above when summarizing the cv.glmnetr() output due to random data partitions for the CV folds.

More example data and relaxed lasso fits

The glmnetr.simdata() can be used to obtain example data not only survival analyses but also for linear models and logistic models. The glmnetr.simdata() output object list contains not only xs for the predictor matrix, yt for time to event or censoring and event for event indication but also y_ for a normally distributed random variable for the linear model setting and yb for the logistic model setting. Below we show examples extracting and analyzing simulated data and for the linear model and logistic model structures.

```
##
##
     The relaxed minimum is obtained for lambda = 0.03319184, index = 44 and gamma = 0.5
##
     with df (number of non-zero terms) = 47, average deviance = 1.114769 and beta =
##
              Х4
                             Х5
                                             X8
                                                           X10
                                                                         X11
##
    1.161532e+00 -1.549189e+00
                                  3.223005e-02 -3.006510e-01
                                                                2.265790e-01
             X12
                                                           X17
##
                            X14
                                           X16
                                                                         X18
##
    1.196422e-01
                   1.067253e+00
                                 -8.194970e-01
                                                 7.280095e-14
                                                                1.269236e+00
##
             X19
                            X20
                                           X21
                                                           X22
                                                                         X23
    3.782328e-01
                  -1.159691e-01
                                  4.013828e-01
                                                -5.696146e-01
##
                                                                3.107055e-01
##
             X24
                            X25
                                           X31
                                                           X34
                                                                         X38
##
    3.021748e-01
                   1.820749e+00
                                 -2.789714e-02
                                                -4.220347e-02
                                                               -1.858647e-02
##
             X39
                                           X43
                                                           X44
                            X42
                                                                         X49
##
   -3.955076e-02
                 -5.575306e-02
                                  7.198290e-02 -3.456562e-02
                                                                3.776110e-02
##
             X50
                            X58
                                           X59
                                                           X60
                                                                         X61
##
   -5.184501e-02
                   2.372919e-02
                                  3.930152e-02
                                                 2.669017e-02
                                                                3.428079e-02
##
             X62
                            X63
                                           X67
                                                           X69
                                                                         X72
##
    4.135598e-02
                   2.856378e-02
                                 -1.668165e-02
                                                 3.939001e-02
                                                                4.305880e-02
##
             X74
                            X78
                                           X79
                                                           X83
                                                                         X85
##
    4.264499e-02
                   1.403872e-02
                                 -4.858182e-02
                                                 3.873856e-02
                                                               -3.775158e-02
##
             X87
                            X89
                                           X91
                                                           X93
                                                                         X96
                                  4.623275e-02 5.977543e-02
##
   -4.837261e-02
                   4.738807e-02
                                                                2.214418e-02
##
             X97
                           X100
                   1.903081e-02
##
   -1.800447e-02
##
##
     The fully relaxed (gamma=0) minimum is obtained for lambda = 0.05285079 and index = 39
     with df (number of non-zero terms) = 29, average deviance = 1.129838 and beta =
##
            X4
                         Х5
##
                                     X10
                                                  X11
                                                               X12
                                                                            X14
    1.20081248 -1.56120791 -0.37574751
                                          0.26079629
##
                                                       0.17613590
                                                                    1.22237202
##
           X16
                        X18
                                     X19
                                                  X20
                                                               X21
                                                                            X22
   -0.96787628
                1.28082345
                             0.39684005 -0.13359011
                                                       0.42388504 -0.58702071
```

```
X23
                        X24
                                    X25
                                                 X42
                                                             X43
                                                                          X49
##
                            1.84143659 -0.06802143
##
    0.31994642
                0.31143832
                                                      0.08228061
                                                                  0.04727775
##
           X50
                        X59
                                    X61
                                                 X62
                                                             X72
                                                                          X79
   -0.06763110
                0.05154905
                             0.05362791
                                         0.05577944
                                                      0.04777248 -0.06587503
##
##
           X85
                        X87
                                    X89
                                                 X91
                                                             X93
   -0.05354526 -0.06693239
                             0.05407041
                                         0.06285454
##
                                                      0.07167155
##
     The UNrelaxed (gamma=1) minimum is obtained for lambda = 0.01899359 and index = 50
##
##
     with df (number of non-zero terms) = 68, average deviance = 1.11494
##
##
##
     Order coefficients entered into the lasso model (1st to last):
    [1] "X25"
               "X18"
                      "X5"
                                     "X22"
                                            "X21"
##
                              "X4"
                                                    "X19"
                                                           "X23"
                                                                  "X24"
                                                                          "X14"
  [11] "X20"
               "X7"
                       "X11"
                              "X16"
                                     "X10"
                                            "X43"
                                                    "X79"
                                                           "X12"
                                                                  "X50"
                                                                          "X93"
  [21] "X42"
               "X62"
                       "X87"
                              "X89"
                                     "X91"
                                             "X49"
                                                    "X72"
                                                           "X59"
                                                                   "X61"
                                                                          "X85"
   [31] "X39"
               "X44"
                       "8X"
                              "X34"
                                     "X74"
                                             "X83"
                                                    "X69"
                                                           "X31"
                                                                   "X38"
                                                                          "X63"
   [41] "X96"
               "X58"
                       "X60"
                              "X67"
                                     "X78"
                                            "X97"
                                                    "X100" "X51"
                                                                  "X75"
                                                                          "X6"
  [51] "X48"
               "X80"
                       "X82"
                              "X36"
                                     "X57"
                                            "X26"
                                                    "X52"
                                                           "X35"
                                                                  "X45"
                                                                          "X54"
## [61] "X56"
               "X65"
                       "X71"
                              "X73"
                                     "X90"
                                            "X94"
                                                    "X46"
                                                           "X70"
# plot(cv.lin.fit, coefs=TRUE)
# extract logistic regression model data
                        # just as a comment as we did this above
\# xs = simdata\$xs
vb = simdata$vb
                        # vector of binomial (0 or 1) outcomes
# run a logistic regression lasso model
cv.bin.fit = suppressWarnings(cv.glmnetr(xs,NULL,yb,NULL,family="binomial",track=0))
summary(cv.bin.fit)
##
##
     The relaxed minimum is obtained for lambda = 0.03486156, index = 22 and gamma = 0
     with df (number of non-zero terms) = 9, average deviance = 0.611035 and beta =
##
                                            X19
##
           X4
                      Х5
                                 X18
                                                        X21
                                                                   X22
                                                                               X23
    1.8117021 -2.7690157
                          1.9554297 0.5723943 0.7843262 -0.7148489 0.3575476
##
##
                     X25
          X24
##
    0.4489259 2.6955189
##
##
     The fully relaxed (gamma=0) minimum is obtained for lambda = 0.03486156 and index = 22
     with df (number of non-zero terms) = 9, average deviance = 0.611035 and beta =
##
##
           Х4
                      Х5
                                 X18
                                            X19
                                                        X21
                                                                   X22
                                                                               X23
##
    1.8117021 -2.7690157
                           1.9554297
                                     0.3575476
##
          X24
                      X25
    0.4489259 2.6955189
##
##
##
     The UNrelaxed (gamma=1) minimum is obtained for lambda = 0.00653242 and index = 40
     with df (number of non-zero terms) = 53, average deviance = 0.618209
##
##
##
     Order coefficients entered into the lasso model (1st to last):
                                                           "X24"
                       "X5"
                                     "X21"
                                            "X22"
                                                                   "X23"
##
    [1] "X25"
               "X18"
                              "X4"
                                                    "X19"
                                                                          "X20"
   [11] "X49"
               "X11"
                       "X39"
                              "X68"
                                     "X7"
                                             "X10"
                                                    "X14"
                                                           "X47"
                                                                   "X35"
                                                                          "X50"
   [21] "X69"
               "X37"
                      "X42"
                              "X61"
                                     "X79"
                                            "X91"
                                                    "X54"
                                                           "X40"
                                                                  "X63"
                                                                          "X93"
  [31] "X32"
               "X72"
                       "X82"
                              "X16"
                                     "X31"
                                             "X92"
                                                    "X100" "X34"
                                                                   "X51"
                                                                          "X85"
## [41] "X41"
               "X67"
                       "X81"
                              "X30"
                                     "X44"
                                             "X66"
                                                    "X74"
                                                                   "X9"
                                                           "X84"
                                                                          "X52"
```

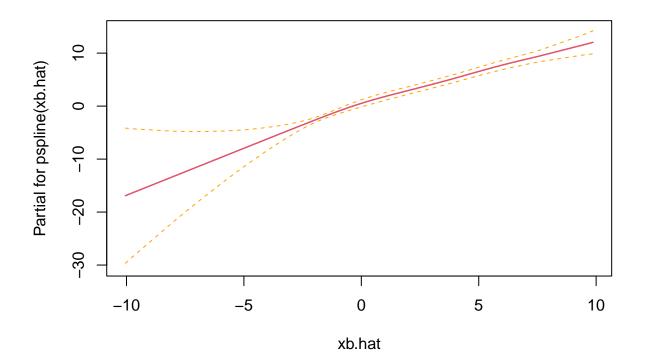
```
## [51] "X55" "X36" "X38"
```

```
# plot(cv.bin.fit, coefs=TRUE)
```

Further model assessment

One can also fit a spline to the predicteds obtained form the predict functions. This may help to understand nonlinearities in the predicteds, but may also give inflated hazard ratios.

```
# Get predicteds from CV relaxed lasso model embedded in nested CV outputs & Plot
xb.hat = predict( object=cv.cox.fit , xs_new=xs, lam=NULL, gam=NULL, comment=FALSE)
# describe the distribution of xb.hat
round(1000*quantile(xb.hat,c(0.01,0.05,0.1,0.25,0.5,0.75,0.90,0.95,0.99)))/1000
##
       1%
              5%
                    10%
                           25%
                                  50%
                                          75%
                                                 90%
                                                        95%
                                                               99%
## -5.912 -4.444 -3.633 -1.904
                                0.039
                                       1.915
                                              3.454
                                                      4.615
# Fit a spline to xb.hat uisng coxph, and plot
fit1 = coxph(Surv(y_, event) ~ pspline(xb.hat))
termplot(fit1,term=1,se=TRUE)
```



From this spline fit we see the predicteds are approximately linear with the log hazard ratio.