An Overview of glmnetr

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The Package

The nested.glmnetr() function of the 'glmnetr' package allows the user to fit multiple machine learning models on a common dataset with a single function call allowing an efficient comparison of different modeling approaches. Additionally this function uses cross validation (CV) to estimate model performances for these different modeling approaches. As most of these machine learning models choose hyperparameters informed by a cross validation or some sort of out of bag (OOB) performance measure, the nested.glmnetr() function provides model performance estimates based upon either a nested cross validation (NCV) or analogous approach. Measures of model performance include concordances for survival time and binomial outcomes and R-squares for quantitative numeric outcomes, as well as deviance ratios, i.e. 1-deviance(model)/deviance(nullmodel), and linear calibration coefficients. Too often one sees performance reports including things like sensitivity, specificity or F1 scores in absence of any consideration of calibration. Whereas linear calibration does not exhaust the needs of calibration considerations, it does provide a first high level insight. As the purpose of the nested.glmnetr() function is to not only describe performance but to derive the models, each of the fitted models as well as performance measures are stored in a single output object.

The nested.glmnetr() function fits cross validation informed Relaxed lasso, ridge, gradient boosting machine ('xgboost'), Random Forest ('RandomForestSRC'), Artificial Neural Network (ANN), Recursive Partitioning ('RPART') and step wise regression models. As run times may be long, the user specifies which of these models to fit. By default only the lasso model suite is fit, including the (standard) lasso, relaxed lasso, fully relaxed lasso (gamma=0) and the ridge regression models. (The program was originally written to simply compare the lasso and stepwise regression models and thus this inclusion of the lasso by default, as well as the program name.) By default model performances are calculated using cross validation but if the goal is to only fit the models this can be done using the option do_ncv=0.

As with the 'glmnet' package, tabular and graphical summaries can be generated using the summary and plot functions. Use of the 'glmnetr' package has many similarities to the 'glmnet' package and the user may benefit by a review of the documentation for 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.

For some datasets, for example when the design matrix is not of full rank, 'glmnet' may have very long run times when fitting the relaxed lasso model, from our experience when fitting Cox models on data with many predictors and many patients, making it difficult to get solutions from either glmnet() or cv.glmnet(). This may be remedied with the 'path=TRUE' option when calling cv.glmnet(). In the 'glmnetr' package we always take an approach like that of path=TRUE.

When 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.

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 in vector form. For the different machine learning modeling approaches the package is set up to model generalizations of the Cox proportional hazards survival model, the "binomial" outcome logistic model and linear regression for well behave numerical outcomes treated as if "guassian" in distribution. When fitting the Cox model the outcome model variable is interpreted as the "time" variable, and one must also specify 3) a variable for event, again 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.

The input vectors may optionally be specified as column matrices (with only one column each) in which case the column name will be kept and expressed in the model summaries.

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 for relaxed lasso fit of survival data
# First, optionally, assign a seed for random number generation to get replicable 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
cat(dim(xs))
```

```
## 1000 100
```

```
# Check the rank of the design matrix, i.e. the degrees of freedom in the predictors
# using function from the Matrix package
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         X20
##  [1,]  1  1  0  0  0  0  0  0  0   1   0   1  0.1513225 -0.4034383  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  1  0  0   0   0   0 -0.3292269  0.3086399 -0.48443836
##  [4,]  1  1  0  0  0  0  0  0  0   1   0   0  2.0635214 -0.5500741 -0.02173104
##  [5,]  1  0  0  0  1  0  0  1  0   0   0   0  0.3905722 -0.6836452 -0.37643201
##  [6,]  1  0  1  0  0  0  0  0  1   0   0   0 -0.2397597  1.6909447  0.49599945
##  [7,]  1  0  1  0  0  0  0  1  0   0   0   0 -0.5592424  0.2314638 -0.53198341
##  [8,]  1  0  0  1  0  0  0  0  0   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
## [10,]  1  0  0  0  1  0  0  0  1   0   0   0 -0.3079151 -0.6105910 -0.88711869
```

Performance of cross validation (CV) informed relaxed lasso model

Because the values for lambda and gamma informed by CV are specifically chosen to give a best fit, model fit statistics for the CV informed 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). We demonstrate the model performance evaluation by nested cross validation first for the lasso models with the evaluation of other machine learning models being similar. For this performance evaluation we use the nested.glmnetr() function which first fits lasso models based upon all data and then performs the cross validation for calculation of concordances or R-squares, deviance ratios and linear calibration summaries.

```
set.seed(465783345)
nested.cox.fit = nested.glmnetr(xs, NULL, y_, event, family="cox",
                                dolasso=1, dostep=1, steps_n=40, folds_n=10, 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. We suppress these warnings here. The first term in the call to nested.glmnetr(), xs, is the design matrix for predictors. The second input term, here given the value NULL, is for the start time in case the (start, stop) time data setup is used in a Cox survival model fit. The third term, here y_, 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. If one sets track=1 the program will update progress in the R console, else for track=0 it will not.

As usual with R functions and packages we use the summary function to describe output. Here the summary function displays a brief summary of the input data and program options before proceeding to describe model performances. The data summary includes sample size, number of events, number of candidate model predictors, degress of freedom in these predictors as well as average deviance and some average minus 2 log likelihoods. Model performances are displayed for the different lasso models, e.g. standard, relaxed, fully relaxed as well as the ridge regression and stepwise regression models. Hyperparamters considered for stepwise regression were degress of freedom (df) and p, the p-value for entry into the regression equation, as discussed by JWHT (James, Witten, Hastie and Tibshirani, An Introduction to Statistical Learning with applications in R, 2nd ed., Springer, New York, 2021). Performance measures include deviance ratio, linear calibration coefficients and measures of agreement, here for the Cox model framework concordance. Additionally there are the deviance ratio and agreement values from the whole sample.

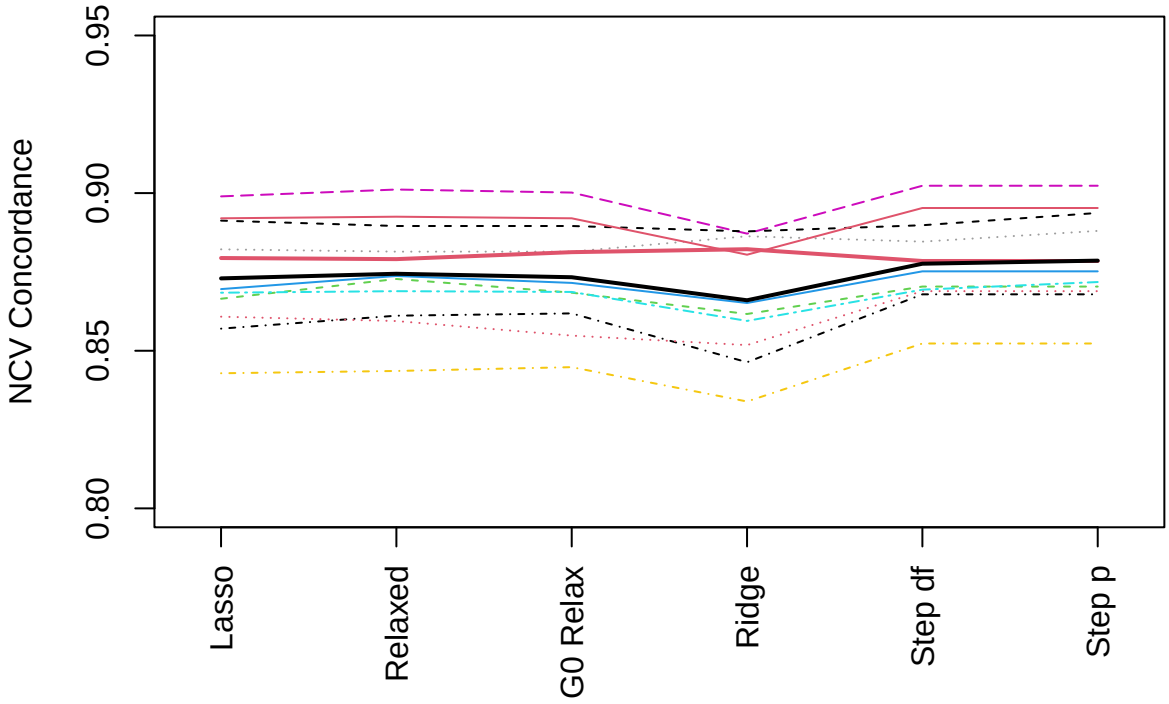
```r
# Summarize relaxed lasso model performance informed by cross validation
summary(nested.cox.fit)
```

```
##
##  Sample information including number of records, events, number of columns in
##  design (predictor, X) matrix, and df (rank) of design matrix:
##               family                    n               nevent
##                  cox                 1000                  698
##           xs.columns                xs.df      null.dev/nevent
##                  100                   94                12.43
## null.m2LogLik/nevent  sat.m2LogLik/nevent
##                12.43                    0
##
##  Tuning parameters for models :
##    folds_n stratified      limit       fine       ties     method    steps_n
##         10          1          1          0      efron     loglik         40
##
##   LASSO: Ave is for (nested) CV model performance summary, else naive summary for
##           fit on all data
##               Ave DevRat Ave Slope Ave Concordance Ave Non Zero Naive Devian
## LASSO min         0.2452    1.0702          0.8730         49.8      10.3217
## LASSO minR        0.2470    1.0083          0.8744         21.0      10.3044
## LASSO minR.G0     0.2435    0.9451          0.8733         17.6      10.2333
## Ridge             0.2256    1.2887          0.8660         99.0      10.2946
##               Naive Concordance Non Zero
## LASSO min                0.8794       44
## LASSO minR               0.8791       19
## LASSO minR.G0            0.8813       14
## Ridge                    0.8822       99
##
##   Stepwise tuned: Ave is for (nested) CV model performance summary, else
##        naive summary for fit on all data
##                   Ave DevRat Ave Slope Ave Concordance Ave Non Zero
## Stepwise df tuned     0.2541    0.9741          0.8776         14.7
## Stepwise p tuned      0.2549    0.9775          0.8786         15.0
##                   Naive Devian Naive Concordance Non Zero
## Stepwise df tuned      10.3034            0.8785       15
## Stepwise p tuned       10.3034            0.8785       15
```

From this output we also see the number of non-zero coefficients in the different models, reflecting model complexity at least for the lasso model, along with the linear calibration coefficients obtained by regressing the outcome on the predicteds.

Model performance measures from the nested cross validation (NCV) can also be visualized with a plot which shows the calculated performances for the individual folds of the cross validation.

```
# Summarize relaxed lasso model performance informed by cross validation
plot(nested.cox.fit, type="agree", ylim=c(0.8,0.95))
```



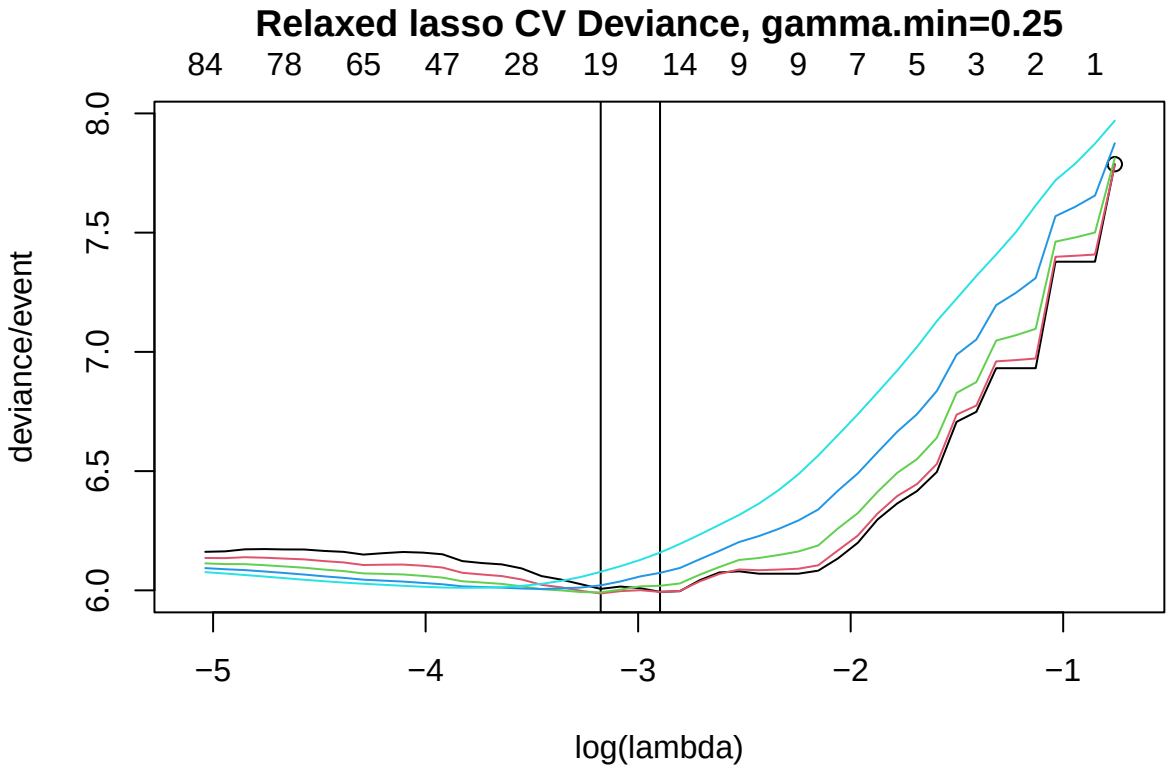
The performance measure estimates, here of concordance, from the individual (outer) cross validation for each fold are depicted by thin lines of different colors and styles, while the composite value from all folds is depicted by a thicker black line, and the performance estimates naively calculated on all data, the same as the data used for model derivation, are depicted in a thicker red line. Here we see that the performance measures for the different models are quite variable across the folds, yet highly correlated with each other. Also, as expected the concordance for the model derived uisng the the full dataset, naively calculated on the same data (i.e. the full data set) as used in model derivation, are larger than the average of the concordances from the different folds. Plots can also be constructed using option "devrat" for deviance ratios, "intcal" for linear calibration intercept coefficients and "lincal" for linear calibration slope coefficients.

The CV informed relaxed lasso model fit

As mentioned, the nested.glmnetr() function also derives the models on all data set and stores these for further examination and usage. The choice of lambda and gamma hyperparameters for the relaxed lasso model is based upon a search across two dimensions for the pair that maximizes the likelihood, or similarly minimizes the deviances, as informed by a cross validation. The next plot depicts the deviances across these two dimensions for the full dataset.

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

```
##  min CV average deviance (max log likelihood) for
##    relaxed at log(lambda)  = -3.176, gamma.min = 0.25, df = 19
##    fully relaxed at log(lambda)   = -2.897, df = 14
##    fully penalized at log(lambda) = -3.827, df = 44
```

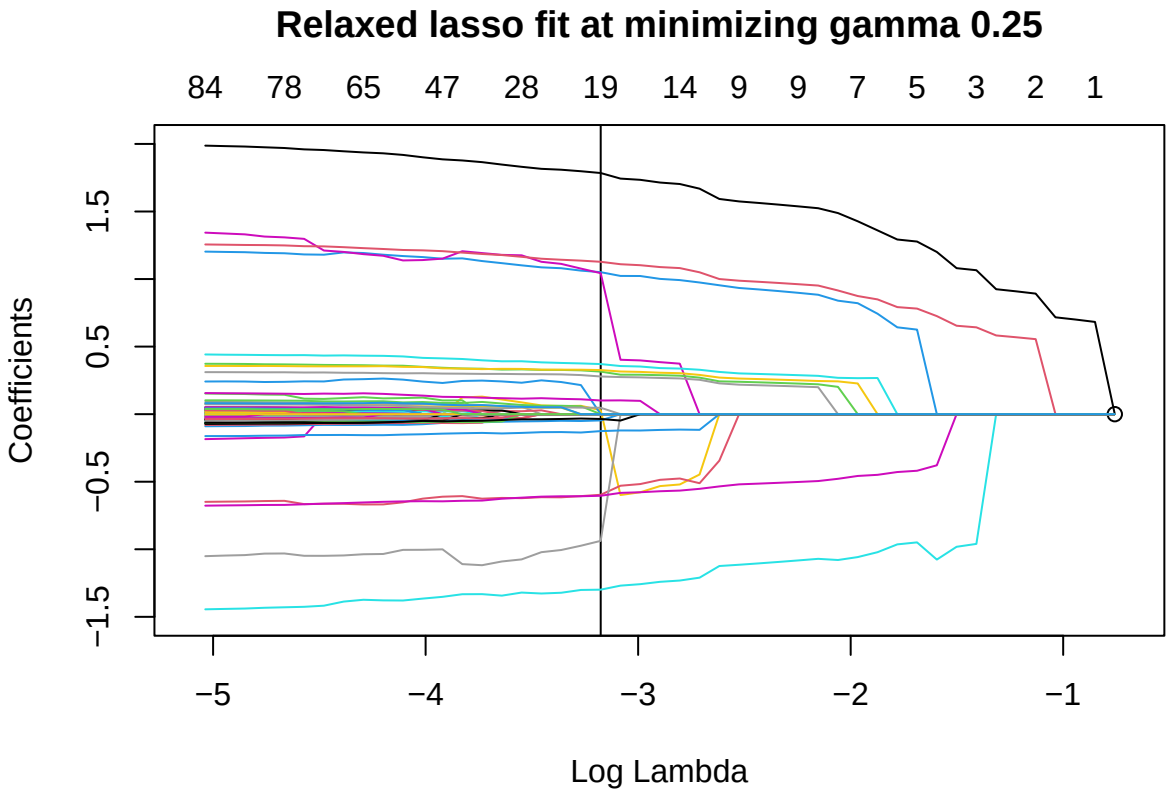


This figure has multiple lines, depicting deviance as a function of lambda for different gamma values. Whereas there is no legend here for gamma, when non-zero coefficients start to enter the model as the penalty is reduced, here shown at the right, deviances tend to be smaller for gamma = 0, greater for gamma = 1 and in between for other gammas values. The minimizing lambda and gamma pair is indicated by the left most vertical line, here about log(lambda) = -3.18. The minimizing lambda can be read from the horizontal axis. Because the different lines depicting deviances for the different values of gamma can be nearly overlapping, the minimizing gamma is described in the title, here 0.25. From this figure we also see that at log(lambda)=-3.18 the deviance is hardly distinguishable for gamma ranging from 0 to 0.5. More relevant we see that the fully unpenalized lasso model fits (gamma=0) shown in a black line with a black circle at the largest lambda, achieve a minimal deviance for about a log(lambda) of -2.9, and highlighted by the right most vertical line. The minimizing deviance for the fully relaxed lasso model is nearly that of the relaxed lasso model tuning for both lambda and gamma.

A plot depicting model fits as a function of lambda is given in the next figure.

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

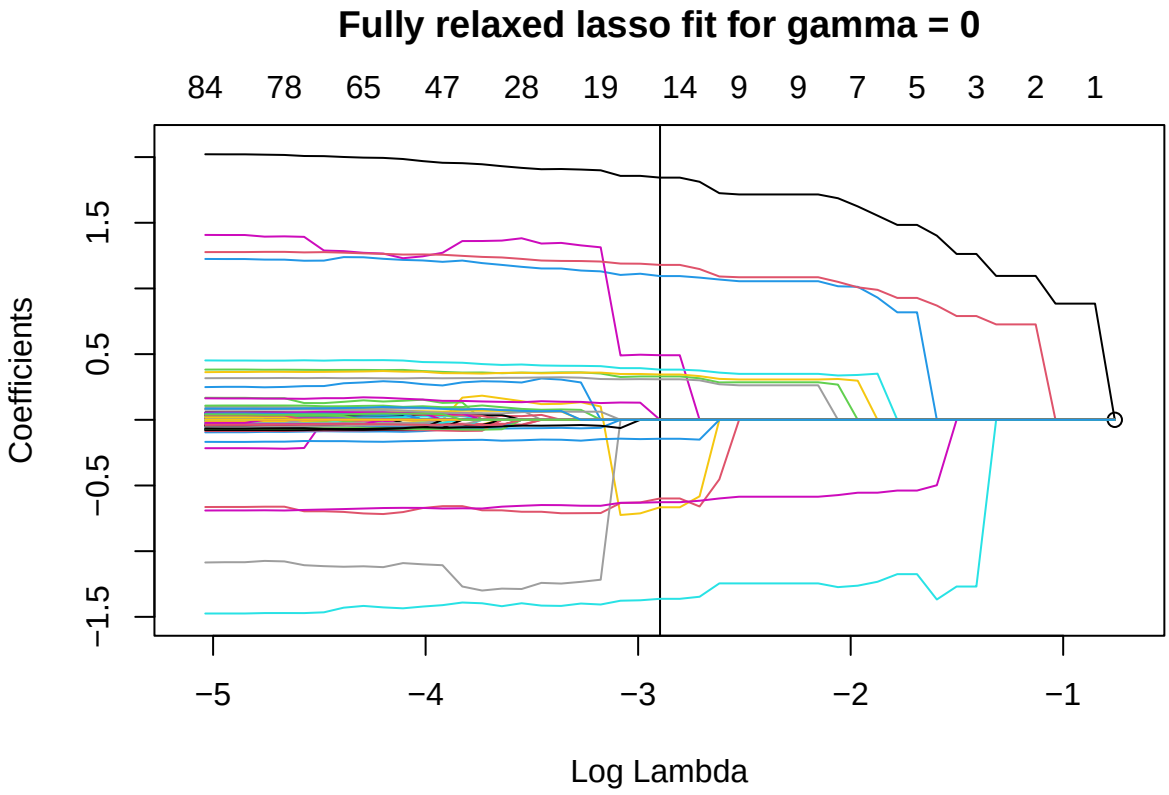
```
##  min CV average deviance (max log likelihood)
##   at log(lambda.min) = -3.176, gamma.min = 0.25, df = 19
```



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=0.25 as noted in the tile, and the minimizing lambda indicated by the vertical line. 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(nested.cox.fit, coefs=TRUE, gam=0)
```

```
##  Fully relaxed min CV average deviance (max log likelihood)
##   at log(lambda.min) = -2.897, df = 14
```



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, 14, to be substantially less than the 19 from the relaxed lasso fit and the 44 from the fully penalized lasso fit.

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

A summary of the actual lasso model fit can be gotten by using the cvfit=1 option in the summary() call.

```
# Summarize relaxed lasso model fit informed by cross validation
summary(nested.cox.fit, cvfit=1)
```

```
##
##   The relaxed minimum is obtained for lambda = 0.04174656 , index = 27 and gamma = 0.25
##   with df (number of non-zero terms) = 19, average deviance = 5.987085 and beta =
##           X4           X5           X7           X10          X14
##  1.050952e+00 -1.298945e+00  2.912949e-02 -5.966936e-01  1.043615e+00
##          X15          X16          X18          X19          X20
## -1.719568e-16 -9.378331e-01  1.127645e+00  3.149391e-01 -1.253247e-01
##          X21          X22          X23          X24          X25
##  3.707304e-01 -6.039354e-01  3.263490e-01  2.789101e-01  1.784703e+00
##          X38          X60          X88          X97
##  1.011793e-01 -4.634282e-02  4.740086e-02 -3.554883e-02
##
##   The fully relaxed (gamma=0) minimum is obtained for lambda = 0.0551865 and index = 24
##   with df (number of non-zero terms) = 13, average deviance = 5.993744 and beta =
##         X4         X5         X7        X10        X14        X18        X19
##  1.0941352 -1.3627747 -0.6659735 -0.5988756  0.4916291  1.1792301  0.3302211
##        X20        X21        X22        X23        X24        X25
## -0.1444546  0.3820778 -0.6270995  0.3448224  0.3085746  1.8435742
##
##   The UNrelaxed (gamma=1) minimum is obtained for lambda = 0.02176669 and index = 34
##   with df (number of non-zero terms) = 44, average deviance = 6.010734
##
##
##   Order coefficients entered into the lasso model (1st to last):
##  [1] "X25"  "X18"  "X5"   "X22"  "X4"   "X21"  "X23"  "X19"  "X24"  "X10"
## [11] "X7"   "X20"  "X14"  "X38"  "X97"  "X16"  "X60"  "X88"  "X12"  "X43"
## [21] "X71"  "X100" "X34"  "X32"  "X50"  "X58"  "X41"  "X49"  "X64"  "X84"
## [31] "X91"  "X98"  "X39"  "X40"  "X66"  "X73"  "X74"  "X11"  "X61"  "X69"
## [41] "X70"  "X96"  "X63"  "X77"
```

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 use the predict() function to get the coefficients for the lasso model, which is done by not specifying a predictor matrix. If one specifies a new design predictor matrix xs_new, then the predicteds xs_new*beta are generated. When used to extract the model coefficients, the predict() function provides an output object in vector form (actually a list with two vectors) and so can easily be used for further calculations. By default the predict() 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 here.

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

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

```
# Print out the non-zero coefficients
beta$beta
```

```
##            X4            X5            X7           X10           X14
##  1.050952e+00 -1.298945e+00  2.912949e-02 -5.966936e-01  1.043615e+00
##           X15           X16           X18           X19           X20
## -1.719568e-16 -9.378331e-01  1.127645e+00  3.149391e-01 -1.253247e-01
##           X21           X22           X23           X24           X25
##  3.707304e-01 -6.039354e-01  3.263490e-01  2.789101e-01  1.784703e+00
##           X38           X60           X88           X97
##  1.011793e-01 -4.634282e-02  4.740086e-02 -3.554883e-02
```

```
# Print out all coefficients
beta$beta_
```

```
##            X1            X2            X3            X4            X5
##  0.000000e+00  0.000000e+00  0.000000e+00  1.050952e+00 -1.298945e+00
##            X6            X7            X8            X9           X10
##  0.000000e+00  2.912949e-02  0.000000e+00  0.000000e+00 -5.966936e-01
##           X11           X12           X13           X14           X15
##  0.000000e+00  0.000000e+00  0.000000e+00  1.043615e+00 -1.719568e-16
##           X16           X17           X18           X19           X20
## -9.378331e-01  0.000000e+00  1.127645e+00  3.149391e-01 -1.253247e-01
##           X21           X22           X23           X24           X25
##  3.707304e-01 -6.039354e-01  3.263490e-01  2.789101e-01  1.784703e+00
##           X26           X27           X28           X29           X30
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X31           X32           X33           X34           X35
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X36           X37           X38           X39           X40
##  0.000000e+00  0.000000e+00  1.011793e-01  0.000000e+00  0.000000e+00
##           X41           X42           X43           X44           X45
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X46           X47           X48           X49           X50
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X51           X52           X53           X54           X55
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X56           X57           X58           X59           X60
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00 -4.634282e-02
##           X61           X62           X63           X64           X65
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
```

```
##           X66           X67           X68           X69           X70
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X71           X72           X73           X74           X75
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X76           X77           X78           X79           X80
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X81           X82           X83           X84           X85
##  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00  0.000000e+00
##           X86           X87           X88           X89           X90
##  0.000000e+00  0.000000e+00  4.740086e-02  0.000000e+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 -3.554883e-02  0.000000e+00  0.000000e+00  0.000000e+00
```

```
# Get the predicteds (linear predictors) for the original data set
predicteds = predict(nested.cox.fit, xs)
```

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

```
# Print out the first few predicteds
predicteds[1:20]
```

```
##  [1] -0.6446191 -3.4901590  4.3166516  1.3425973 -0.1500069  1.2901788
##  [7] -3.8608813  0.3456247  6.1151657  1.5431362  1.0919012 -1.7379752
## [13]  0.7941607  2.7537587 -0.6522066  0.5313555  0.8459184  3.3600472
## [19] -2.4937645  1.9657998
```

Nested cross validation (NCV) for multiple models

Here we evaluate multiple machine learning models, in particular the lasso, ridge, XGB, random forest and neural network models. For this example too we perform an analysis for the generalizations of linear regression in contrast to the Cox model in the last example. The glmnetr.simdata() function used above actually creates an output object list contains not only xs for the predictor matrix, yt for time to event or censoring and and an event indicator but also y_ for a normally distributed random variable for the linear model setting and yb for the logistic model setting.

```
# Nested cross validation evaluating a machine learning model suite with guassian errors
# Use the same simulated data output object from above, that is from the call
# simdata=glmnetr.simdata(nrows=1000, ncols=100, beta=NULL)
#
# extract linear regression model data
yg = simdata$y_                              # outcome vector with Gaussian (normal) errors
# Get the ML model fits
nested.gau.fit = nested.glmnetr(xs,NULL,yg,NULL,family="gaussian",
      dolasso=1, doxgb=list(nrounds=250), dorf=1, doann=1, ensemble=c(1,0,0,0, 0,1,0,1),
      folds_n=10, seed=219301029, track=0)
```

```r
# Summarize the results
summary(nested.gau.fit)
```

```
##
##  Sample information including number of records, number of columns in
##  design (predictor, X) matrix, and df (rank) of design matrix:
##          family               n      xs.columns           xs.df      null.dev/n
##        gaussian            1000             100              94            8.09
## null.m2LogLik/n  sat.m2LogLik/n
##            8.09               0
##
##  Tuning parameters for models :
##    folds_n stratified      limit       fine       ties
##         10          1          1          0      efron
##
##  Tuning parameters for  ANN lasso terms, weights reset  model :
##  n.folds epochs length.Z1 length.Z2 actv drpot  mylr wd l1 lscale scale
##       10    200        18        10    1     0 0.001  0  0      5     1
##
##   LASSO: Ave is for (nested) CV model performance summary, else naive summary for
##           fit on all data
##                Ave DevRat Ave Int Ave Slope Ave R-square Ave Non Zero
## LASSO min         0.8607 -0.0192    1.0184       0.8612         61.2
## LASSO minR        0.8594 -0.0148    1.0137       0.8596         39.6
## LASSO minR.G0     0.8570  0.0059    0.9899       0.8569         29.5
## Ridge             0.8492 -0.0822    1.0979       0.8568         99.0
##               Naive Devian Naive R-square Non Zero
## LASSO min           0.9761          0.938       66
## LASSO minR          0.9761          0.938       66
## LASSO minR.G0       0.9423          0.940       26
## Ridge               0.9660          0.940       99
##
##   XGBoost: Ave is for (nested) CV model performance summary, else naive summary for
##             fit on all data
##                    Ave DevRat Ave Int Ave Slope Ave R-square Ave Non Zero
## XGB Simple            0.7076 -0.1024    1.1252       0.7174          100
## XGB Feature           0.8127 -0.0260    1.0219       0.8136          100
## XGB Offset            0.8562  0.0103    0.9899       0.8562          100
## XGB Tuned             0.8119 -0.0432    1.0675       0.8158          100
## XGB Tuned Feature     0.8510 -0.0358    1.0367       0.8527          100
## XGB Tuned Offset      0.8595  0.0039    0.9925       0.8595          100
##                   Naive Devian Naive R-square Non Zero
## XGB Simple              0.0068         0.9992      100
## XGB Feature             0.0177         0.9979      100
## XGB Offset              0.8712         0.8923      100
## XGB Tuned               0.6976         0.9187      100
## XGB Tuned Feature       0.8590         0.8962      100
## XGB Tuned Offset        0.9716         0.8799      100
##
##   Random Forest: Ave is for CV model performance summary, else naive
##                     summary for fit on all data
##                  Ave DevRat Ave Int Ave Slope Ave R-square Ave Non Zero
## RF Simple            0.7111 -0.2391    1.2184       0.7370           58
```

```
## RF lasso Feature     0.8487 -0.0501    1.0302       0.8497           61
## RF lasso Offset      0.8585  0.0079    0.9903       0.8589           23
##                  Naive Devian Naive R-square Non Zero
## RF Simple                0.5749         0.9499       60
## RF lasso Feature         0.2849         0.9674       61
## RF lasso Offset          0.2934         0.9647       10
##
##   Artificial Neural Network: Ave is for (nested) CV model performance summary,
##         else naive summary for fit on all data
##                                  Ave DevRat Ave Int Ave Slope Ave R-square
## ANN Uninformed                       0.6879  0.1038    0.9464       0.6948
## ANN lasso terms, lasso features      0.8312 -0.0152    0.9761       0.8326
## ANN lasso terms, weights reset       0.8586 -0.0461    0.9918       0.8595
##                                  Ave Non Zero Naive Devian Naive R-square
## ANN Uninformed                          100.0       0.3346         0.9588
## ANN lasso terms, lasso features          39.6       0.5963         0.9266
## ANN lasso terms, weights reset           39.6       1.0334         0.8796
##                                  Non Zero
## ANN Uninformed                        100
## ANN lasso terms, lasso features        66
## ANN lasso terms, weights reset         66
```

Here we see a set of machine learning models evaluated together. All evaluations are based upon the same folds for the outer loop of the cross validation. Those models informed by cross validation in identification of hyperparameters, i.e. lasso, neural network and stepwise, use the same folds in the inner cross validation making the comparisons of model performance between models more stable. For the models based upon other random splittings, i.e. random forest, the same seed is set using set.seed() before each model call facilitating replicability of results. The "Non Zero" column is the number of non zero regression coefficients for the lasso and ridge models, and the number of predictors given to the XGB model. For the random forest model "Non Zero" is the number of predictors randomly selected for possible splitting at each node, a hyperparameter. For the ANN models "non Zero" again is the number of terms given to the ANN for training. Note for the 2nd and 3rd ANN models, based upon the user specification of the *ensemble* option in the call to nested.glmnetr(), only those variables with non zero coefficients in the relaxed lasso model are given as input.

One can save the tabled information from a summary to a data frame using the *table* option as in

```
## put the data into a data frame
dframe = summary( nested.gau.fit , table = 0)
```

```
## use the roundperf() function from 'glmnetr' to round so long as it doesn't too
## obscure the original values
## print just the first 4 columns to get a more succinct table
roundperf(dframe, digits = 3)[,c(1:4)]
```

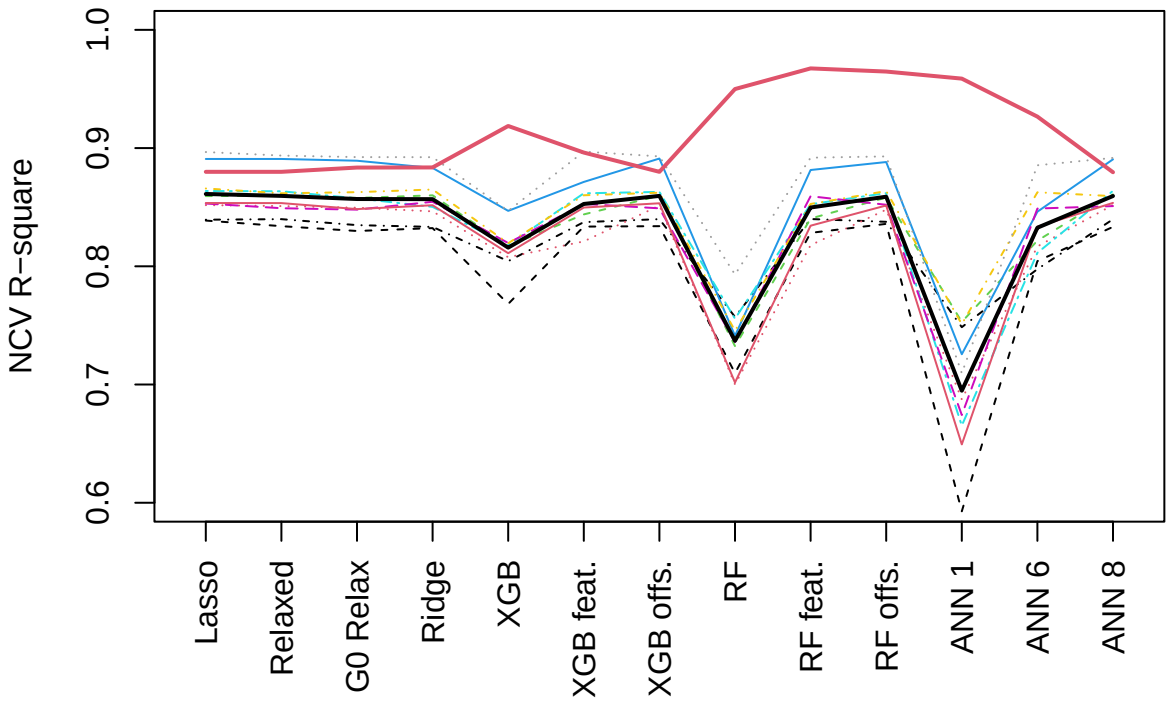
```
##                                  Ave DevRat Ave Int Ave Slope Ave R-square
## LASSO min                            0.861  -0.019     1.018        0.861
## LASSO minR                           0.859  -0.015     1.014        0.860
## LASSO minR.GO                        0.857   0.006     0.990        0.857
## Ridge                                0.849  -0.082     1.098        0.857
## XGB Simple                           0.708  -0.102     1.125        0.717
## XGB Feature                          0.813  -0.026     1.022        0.814
## XGB Offset                           0.856   0.010     0.990        0.856
## XGB Tuned                            0.812  -0.043     1.068        0.816
```

```
## XGB Tuned Feature                    0.851  -0.036     1.037        0.853
## XGB Tuned Offset                     0.859   0.004     0.992        0.860
## RF Simple                            0.711  -0.239     1.218        0.737
## RF lasso Feature                     0.849  -0.050     1.030        0.850
## RF lasso Offset                      0.859   0.008     0.990        0.859
## ANN Uninformed                       0.688   0.104     0.946        0.695
## ANN lasso terms, lasso features      0.831  -0.015     0.976        0.833
## ANN lasso terms, weights reset       0.859  -0.046     0.992        0.859
```

This may be helpful when wanting to further process the findings or incorporate into reports.

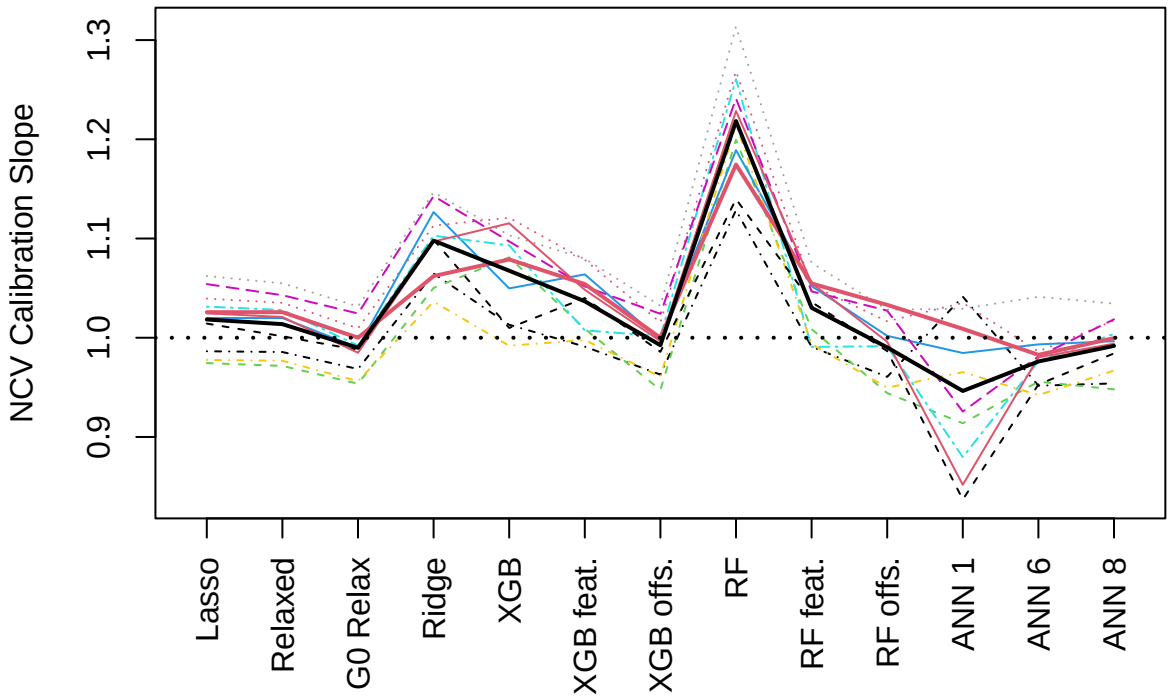
Model performance measures from the nested cross validation can be plotted individually as in here shown for R-square, a measurement of agreement

```
# Summarize relaxed lasso model performance informed by cross validation
plot(nested.gau.fit, type="agree", pow=2, ylim=c(0.6,1))
```



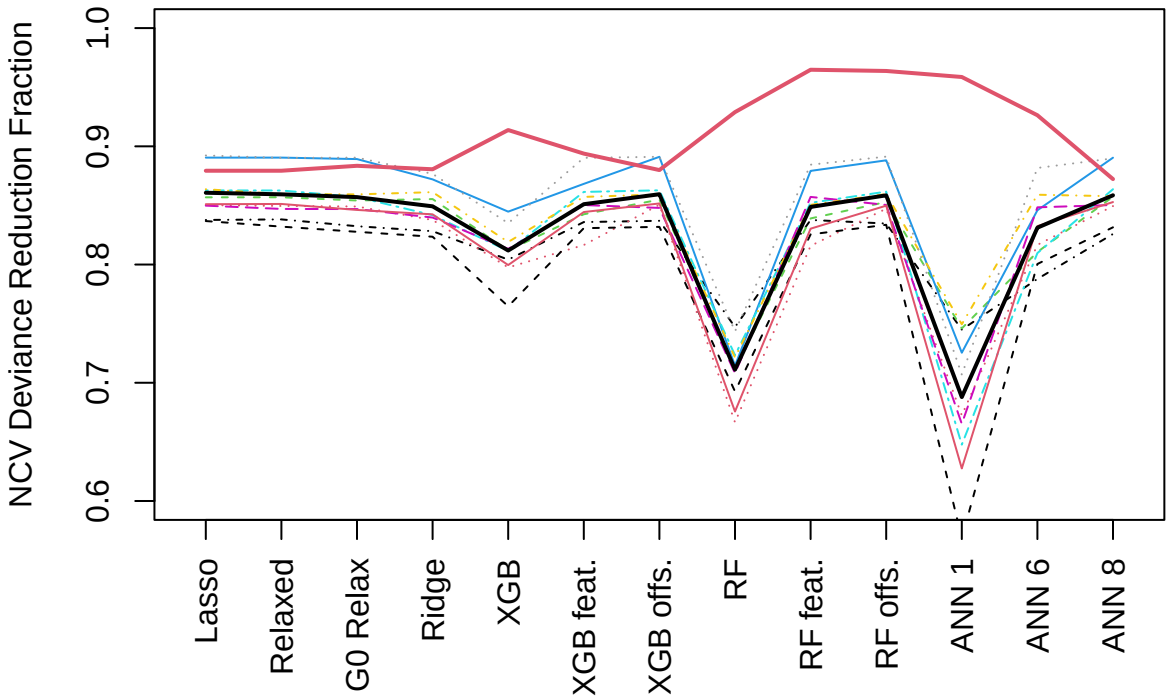
or the linear calibration slope coefficient,

```
# Summarize relaxed lasso model performance informed by cross validation
plot(nested.gau.fit, type="lincal")
```



or the deviance ratio, i.e. the fraction of the null deviance explained by the models,

```
# Summarize relaxed lasso model performance informed by cross validation
plot(nested.gau.fit, type="devrat", ylim=c(0.6,1))
```



The individual model fits are all captured in the nested.glmnetr() output object with names like cv_glmnet_fit, xgb.simple.fit, xgb.tuned.fit, rf.tuned, cv.stepreg.fit and ann_fit_X with X corresponding to the ensemble designation. cv_glmnet_fit has a similar yet different format to that of cv.glmnet() by including further fit information. The XGB outputs are essentially direct outputs from 'xgboost' xgb.train(), but with added information regarding the seed or fold used in the fit as well as the parameters used in the search for the hyperparamaters using the 'mlrMBO' package. The rf.tuned object contains the output from rfsrc() in the object rf.tuned$rf_tuned along with information used for tuning. The ann_fit_X objects are derived using the R 'torch' package and take on their own format for logistical reasons. See the 'Using ann_tab_cv' vignette. Cross validation information from the individual outer folds are contained in datasets like xx.devian.cv, xx.lincal.cv, xx.agree.cv for further processing by the summary() function or by the user. For example

```
# Manually calculate CV R_square for lasso models
corr.cv = nested.gau.fit$lasso.agree.cv
avecorr = colMeans(corr.cv)
R_square = round( avecorr ^2 , digits = 4)
R_square
```

```
##     1se     min    1seR    minR 1seR.G0 minR.G0   ridge
##  0.8588  0.8612  0.8593  0.8596  0.8602  0.8569  0.8568
```

These numbers are consistent with the output from the summary() call.

Further model assessment

Further model assessment can be made based upon the predicteds from the predict() function. For example, one can model the outcomes based upon a spline for the X*Beta hats from the predicteds. This may help to understand potential nonlinearities in the model, but may also give inflated hazard ratios.

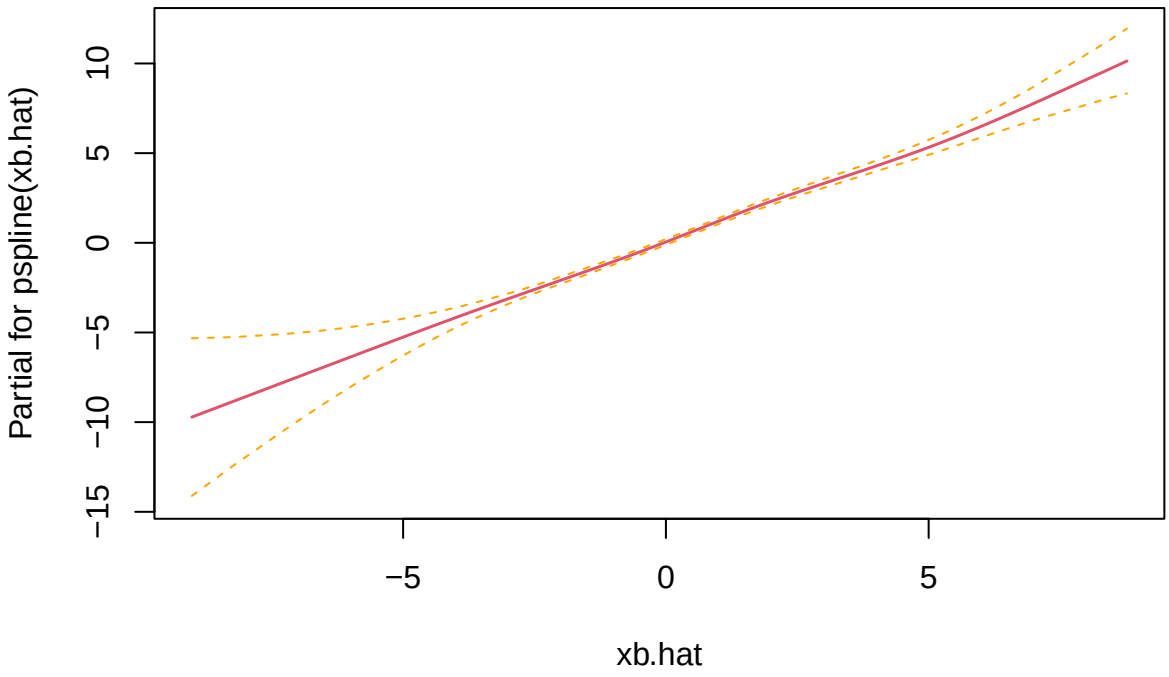
```
# Get predicteds from CV relaxed lasso model embedded in nested CV outputs & Plot
xb.hat = predict( object=nested.cox.fit , xs_new=xs, lam=NULL, gam=NULL, comment=FALSE)
# describe the distribution of xb.hat
round(1000*quantile(xb.hat,c(0.01,0.05,0.1,0.25,0.5,0.75,0.90,0.95,0.99)))/1000
```

```
##     1%     5%    10%    25%    50%    75%    90%    95%    99%
## -5.839 -4.122 -3.233 -1.804 -0.070  1.578  3.188  3.989  5.449
```

```
# Fit a spline to xb.hat uisng coxph, and plot
fit1 = coxph(Surv(y_, event) ~ pspline(xb.hat))
summary(fit1)
```

```
## Call:
## coxph(formula = Surv(y_, event) ~ pspline(xb.hat))
##
##   n= 1000, number of events= 698
##
##                          coef  se(coef) se2     Chisq   DF   p
## pspline(xb.hat), linear 1.073 0.03335  0.03335 1034.93 1.00 4.6e-227
## pspline(xb.hat), nonlin                          3.77 3.04  2.9e-01
##
##              exp(coef) exp(-coef) lower .95 upper .95
## ps(xb.hat)3  7.221e+00  1.385e-01 7.047e-01 7.400e+01
## ps(xb.hat)4  5.215e+01  1.918e-02 8.007e-01 3.396e+03
## ps(xb.hat)5  3.764e+02  2.657e-03 1.508e+00 9.393e+04
## ps(xb.hat)6  2.664e+03  3.754e-04 5.104e+00 1.390e+06
## ps(xb.hat)7  1.634e+04  6.121e-05 2.699e+01 9.886e+06
## ps(xb.hat)8  1.036e+05  9.656e-06 1.791e+02 5.990e+07
## ps(xb.hat)9  9.080e+05  1.101e-06 1.561e+03 5.283e+08
## ps(xb.hat)10 4.941e+06  2.024e-07 8.443e+03 2.892e+09
## ps(xb.hat)11 2.882e+07  3.470e-08 4.875e+04 1.704e+10
## ps(xb.hat)12 2.757e+08  3.627e-09 4.437e+05 1.713e+11
## ps(xb.hat)13 3.015e+09  3.317e-10 4.081e+06 2.228e+12
## ps(xb.hat)14 3.389e+10  2.950e-11 2.878e+07 3.991e+13
##
## Iterations: 4 outer, 16 Newton-Raphson
##      Theta= 0.7383276
## Degrees of freedom for terms= 4
## Concordance= 0.879  (se = 0.005 )
## Likelihood ratio test= 1494  on 4.04 df,   p=<2e-16
```

```
termplot(fit1,term=1,se=TRUE)
```



From this spline fit we see the log hazard ratio is roughly linear in the relaxed lasso predicteds.

Model replicability and model comparisons

To facilitate reproducible results the nested.glmnetr() function stores the seeds used to generate the pseudo random samples used for assigning observations to folds in the outer loop, as well as the fold ids themselves, for all models. Additionally, the program stores the seeds when generating the folds in the inner loop for lasso, XGB, neural network and stepwise regressions as well as the seeds used when generating the bootstrap samples for the random forest models. Using the seeds from a prior call to nested.glmnetr(), one can reproduce the results from this earlier call. Because the seeds are saved for folds both in the inner and outer loop, results can be reproduced even when rerunning an analysis for a single model. If we did not save and manage the seeds the user might have to run all models included in an earlier run to verify or inspect a single model fit. If the seed option is unspecified in the call to nested.glmnetr(), one should be cautious when using set.seed() in one's own code as this too will effect the pseudo randomness used in the ML calculations, which could unwantingly yield identical results when pseudo independent runs are intended.

Using the same folds for the different models controls for some of the variability in the model performance estimates due to the randomness in the choice of folds, which should reduce variability in the differences in performance estimates between different models. nested.glmnetr() stores the model performance measures from each iteration of the outer loop allowing calculation of means and standard deviations (SD) for each model performance measure, as well as differences paired on each fold left out for model derivation in the outer loop. Because of dependencies between the different model fits from a CV loop, there are concerns about the accuracy of the SDs (Bengio Y & Grandvalet Y, "No Unbiased Estimator of the Variance of K-Fold

Cross-Validation", Journal of Machine Learning Research 5 (2004) 1089–1105). Still, people use these SDs routinely as a rough approximation, being cautious of making strong inferences. We expect any dependencies at least between the paired differences should be minimal and reasonable in approximation. This intuition is supported by informal simulations. The reader is invited to perform similar studies using the type of data they encounter.

A simple comparison of model performances based upon agreement can be done as in the example

```
# compare correlations between different models
glmnetr.compcv(nested.gau.fit)
```

```
##
##   Ensemble paramter used when fitting models :
##          ensemble
##     (1,0,0,0, 0,1,0,1)
##
##   Model performance comparison in terms of  Correlation
##
##   Comparison                                    estimate   (95% CI)          p
##
##  lasso.minR  - lasso.min                        -9e-04 (-0.0017, -1e-04)   0.0364
##  lasso.minR  - lasso.minR0                      0.0014 (6e-04, 0.0023)   0.0048
##  lasso.min   - lasso.minR0                      0.0023 (0.0014, 0.0032)   3e-04
##
##  XGBoost (tuned) - XGBoost (simple)            0.0562 (0.0428, 0.0697)   0
##  XGBoost (tuned) lasso feature - no feature    0.0202 (0.0145, 0.026)   0
##  XGBoost (tuned) lasso offset - no offset      0.0239 (0.0201, 0.0277)   0
##
##  RF with lasso feature - no feature            0.0633 (0.0561, 0.0706)   0
##  RF with lasso offset - no offset              0.0683 (0.0589, 0.0777)   0
##
##  ANN with with lasso feature - no feature      0.079 (0.0568, 0.1011)   0
##  ANN with with lasso offset - no offset        0.0935 (0.0728, 0.1143)   0
##
##
##  lasso.minR - XGB (tuned)                      0.0239 (0.0202, 0.0277)   0
##  lasso.minR - XGB with lasso feature           0.0037 (-6e-04, 0.008)   0.084
##  lasso.minR - XGB with lasso offset            0 (-1e-04, 2e-04)   0.8927
##  lasso.minR - Random Forest                    0.0686 (0.059, 0.0782)   0
##  lasso.minR - RF with lasso feature            0.0053 (6e-04, 0.01)   0.0303
##  lasso.minR - RF with lasso offset             0.0018 (4e-04, 0.0033)   0.0205
##  lasso.minR - ANN                              0.0936 (0.0728, 0.1144)   0
##  lasso.minR - ANN l lasso feature              0.0146 (0.0072, 0.0221)   0.0016
##  lasso.minR - ANN l lasso offset (upated)      1e-04 (-5e-04, 6e-04)   0.817
##
##  XGBoost (tuned) - RF                          0.0447 (0.0351, 0.0543)   0
##  XGBoost lasso feature-RF with lasso feature 0.0016 (-0.0013, 0.0045)   0.2404
##  XGBoost lasso offset-  RF with lasso offset 4e-04 (-5e-04, 0.0012)   0.3542
##  XGBoost (tuned) - ANN                           0.0697 (0.051, 0.0884)   0
##  XGBoost lasso feature - ANN, l lasso feature 0.0109 (0.0044, 0.0175)   0.0045
##  XGBoost lasso offset-ANN l lasso offset(upated) 0 (-5e-04, 6e-04)   0.8534
##
##  RF - ANN                                      0.025 (0.0051, 0.0448)   0.0191
##  RF lasso feature - ANN  l lasso feature       0.0093 (0.0022, 0.0165)   0.0163
```

```
##  RF lasso offset - ANN l lasso offset (upated) -3e-04 (-0.0014, 7e-04)   0.5063
```

Note, from Jensens' inequality we expect the R-squares for the different folds to be more biased than the R 's (correlation), and thus calculate the CV estimate for R-square as the (average R from the CV folds) squared instead of average (R-squared from the CVs folds). We also compare agreements for the guassian model by comparing correlations by default, instead of R-squares.

As the outer CV loop performance calculations are saved in the nested.glmntr() output object (with names like lasso.agree.cv, lasso.lincal.cv, xgb.agree.cv, xgb.lincal.cv, etc.) comparisons not provided by glmnetr.compcv() can be calculated from these stored CV data.