

# iEN: integrating mechanistic immunological information into a machine learning framework

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## 1 Licensing

Under the Artistic License, you are free to use and redistribute this software.

## 2 Introduction

Supervised predictive analysis method for flow and mass cytometry data which integrates well known information on cell-signalling responses into the model fitting process. This method is an extension of the well studied Elastic-Net algorithm [2]

Through the prioritization of well understood cell-signalling pathways predictive models of human immunity can more accurately predict responses than the agnostic EN method. The prior knowledge referred to are likelihood coefficients generated by a panel of expert immunologists such that features more consistent with known biology have a higher value with numbers ranging from 0 to 1.

A two-layer K-fold Cross-Validation (CV) approach is used to optimize and estimate model performance in a robust and statistically stringent manner, with the parameter foldid controlling CV behaviour. The models generated by this package are regression model's optimized via grid search during cross-validation

on the provided parameters for `alphaGrid`, `phiGrid`, and `nlambda`. Prediction using the generated "iEN" object will use the mean of out-of-sample models (which is the collection of optimal models generated for each fold of cross-validation) to predict new data, with default prioritization of the new data being the mean of optimal scaling from the K-fold CV.

### 3 Example

This example uses mass cytometry data previously published by Aghaeepour et al [1] which studied the gestational age during pregnancy. Using the data matrix `X` and the vector of prior knowledge, our task is to estimate the vector of gestational age at time of sample collection `Y`.

```
> library(iEN)
> install.packages("caret", repos='http://cran.us.r-project.org')
> library(caret)
> data(test_data)
> alphaGrid <- seq(0,1, length.out=2)
> phiGrid <- exp(seq(log(1),log(10), length.out=2))
> nlambda <- 3
> lambdas=NULL
> ncores <- 2
> eval <- "RSS"
> family <- "gaussian"
> intercept <- TRUE
> standardize <- TRUE
> center <- TRUE
> #define 10-fold cross-validation folds
> temp.folds <- createFolds(unique(foldid),k=10)
> folds <- vector()
> for(k in seq(length(temp.folds))) {
+   folds[which(foldid %in% temp.folds[[k]])] <- k
+ }
> model <- cv_iEN(X, Y, folds, alphaGrid, phiGrid, nlambda, lambdas, priors, ncores, eval, 1)
> Y.hat <- model@cv.preds
> print(model)
```

Estimated model performance, as defined by 'eval' parameter, from out of sample predictions

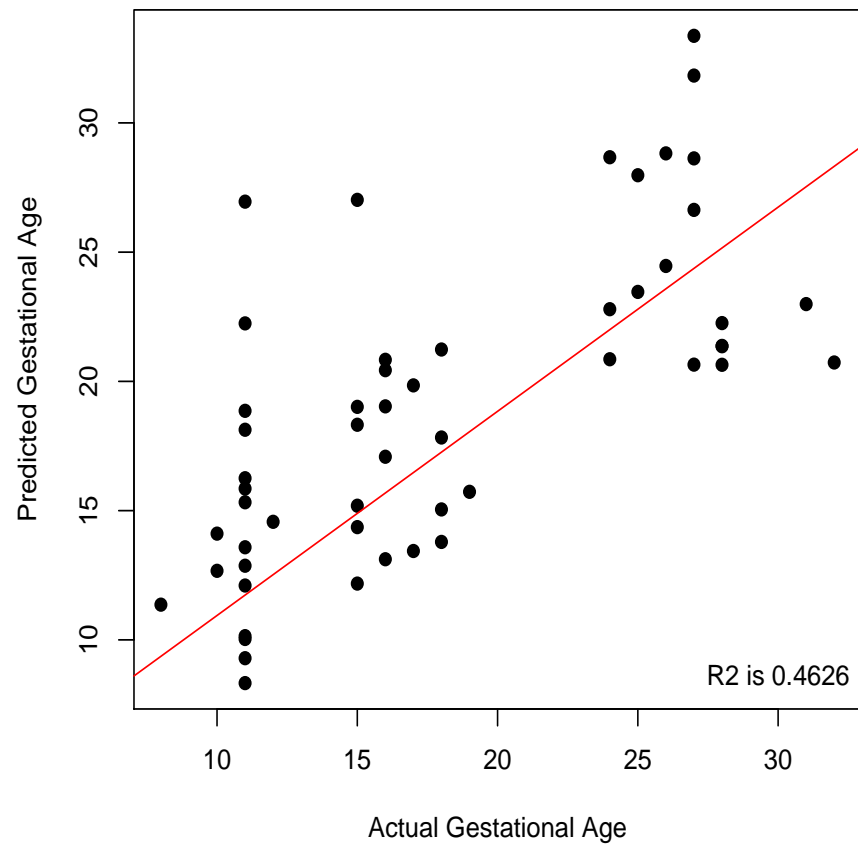
| features | alpha  | lambda    | phi  |
|----------|--------|-----------|------|
| -----:   | -----: | -----:    | ---: |
| 961      | 0      | 0.0000030 | 10   |
| 961      | 0      | 0.2842485 | 1    |
| 961      | 0      | 0.2752201 | 1    |
| 961      | 0      | 0.2884030 | 1    |

|     |   |           |    |
|-----|---|-----------|----|
| 55  | 1 | 0.0010480 | 1  |
| 961 | 0 | 0.3312407 | 1  |
| 961 | 0 | 0.2633111 | 1  |
| 961 | 0 | 0.3020635 | 10 |
| 961 | 0 | 0.3073598 | 1  |
| 961 | 0 | 0.3125372 | 1  |

```

> plot(Y,Y.hat, ylab ="Predicted Gestational Age", xlab="Actual Gestational Age", cex=1.5, p
> abline(fit <- lm(Y ~ Y.hat, ), col='red')
> legend("bottomright", bty="n", legend=paste("R2 is", format(summary(fit)$adj.r.squared, c

```



## References

- [1] Nima Aghaeepour, Edward A Ganio, David McIlwain, Amy S Tsai, Martha Tingle, Sofie Van Gassen, Dyani K Gaudilliere, Quentin Baca, Leslie McNeil, Robin Okada, Mohammad S Ghaemi, David Furman, Ronald J Wong, Virginia D Winn, Maurice L Druzin, Yaser Y El-Sayed, Cecele Quaintance, Ronald Gibbs, Gary L Darmstadt, Gary M Shaw, David K Stevenson, Robert Tibshirani, Garry P Nolan, David B Lewis, Martin S Angst, and Brice Gaudilliere. An immune clock of human pregnancy. *Sci Immunol*, 2(15), sep 2017.
- [2] Hui Zou and Trevor Hastie. Regularization and variable selection via the elastic net. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, apr 2005.