Distributed Lag Interaction Model Overview

Preamble

Installation

The latest version of this package on GitHub can be downloaded and installed by

`install_github("ddemateis/dlim")`

or on CRAN by

`install.packages("dlim")`

Then the package can be loaded by

```
library(dlim)
```

Methodology and Applications

See Demateis et al. 2024 for details on methodology and applications.

Functions in the package

The function `dlim()`

To fit a DLIM using this package, first use the `dlim()` function, which creates a cross-basis using the `cross_basis()` function and then fits a GAM using using the cross-basis. `dlim()` takes a vector of response values, `y`, a matrix of exposure history, `x`, the modifier variable, `modifier`, and a matrix of other covariates, `z`. Do not include the modifier in `z`, as `dlim()` will add the modifier to the covariate matrix later in the function. You will also need to specify the degrees of freedom for the modifier basis, `df_m`, and the exposure time basis, `df_l`. You can optionally specify whether to penalize, `penalize = T` or `penalize = F`, though the function will default to `penalize = T`. By default, `method = "REML"` for penalized models. If the data set is very large, you can set `fit_fn = "bam"` so `dlim()` uses `bam()` instead of `gam()` for model fitting. See `?bam` for more details.

The function `predict()`

After using the `dlim()` function to fit a DLIM, you can use `predict()` to make predictions with confidence intervals for any set of modifying values. `predict()` is an S3 method for objects of class `dlim` which takes an object of class `dlim`, `object`, and the type of prediction, `type = "DLF"` to predict the distributed lag function or point-wise effects for a set of modifier, `type = "CE"` to predict the cumulative effects for a set of modifiers, or `type = c("CE", "DLF")` to predict both the distributed lag function and cumulative effect. You can pass a new vector of modifier values to `newdata`. If left as `NULL`, then prediction will be on the original modifier values. The confidence level can be changed using `alpha`.

The function `plot_cumulative()`

After using the `dlim()` function to fit a DLIM, you can use the `plot_cumulative()` function to plot the cumulative effects and confidence regions for any set of modifying values. `plot_cumulative()` takes a vector of modifying values, `new_modifiers`, and an object of class `dlim`, `mod_fit`. Optionally, you can provide the name of the modifier for the plot axis label, `mod_name`, and a back-transformation function to `mod_trans` if the specified modifier values have been transformed. This function also have the ability to compare a DLM fit to a DLIM fit. If the `dlm_fit` argument is passed a list containing a `crossbasis` object from the `dlnm` package and a fitted DLM model object, then the plot will also include the estimated cumulative effects and confidence region for the same modifying values for the DLM. If the model family is not Gaussian, specify a transformation function using `link_trans`.

The function `plot_DLF()`

After using the `dlim()` function to fit a DLIM, you can use the `plot_DLF()` function to create a grid of plots for the estimated point-wise effects (i.e. estimated distributed lag function) and confidence regions for any set of modifying values. `plot_DLF()` takes a vector of modifying values, `new_modifiers`, an object of class `dlim`, `mod_fit`, and whether to create a grid of plots by modifier value, `plot_by = "modifier"`, or by particular time points, `plot_by = "time"`. If you are want each plot in the grid to be for a time point, you must pass `time_pts` a vector of time points. Optionally, you can provide the name of the modifier for the plot axis label, `mod_name`, and a back-transformation function if the specified modifier values have been transformed. This function also have the ability to compare a DLM fit to a DLIM fit. If the `dlm_fit` argument is passed a list containing a `crossbasis` object from the `dlnm` package and a fitted DLM model object, then the plot will also include the estimated cumulative effects and confidence region for the same modifying values for the DLM. If the model family is not Gaussian, specify a transformation function using `link_trans`.

The function `model_comparison()`

You can use the `model_comparison` function to compare models with and without interaction, or models of varying levels of interaction. See Demateis et al. 2024 for discussion. The `model_comparison` function takes a `dlim` object (must be fit with REML) through the `fit` argument. The fit object is the full model. Options for the null model are a standard DLM with no interaction (`null = "none"`), a DLIM with linear interaction (`null = "linear"`), or a DLIM with quadratic interaction (`null = "quadratic"`). `x` is the exposure matrix used to fit `fit`, `B` is the number of bootstrap samples, and `conf.level` is the confidence level with default 0.95. The function returns a decision to reject or fail to reject based on the confidence level.

Example

Model Fitting

Using the example data set in the package, fit a DLIM using the `dlim()` function. First load the data set:

```
data("ex_data")
str(ex_data)
#> List of 4
#>  $ y       : num [1:1000, 1] 21.4 25.4 22.7 27.2 23.5 ...
#>  $ exposure:Classes 'data.table' and 'data.frame':  1000 obs. of  37 variables:
#>   ..$ PM25_1 : num [1:1000] 11.07 4.84 12.58 14.68 11.36 ...
#>   ..$ PM25_2 : num [1:1000] 13.15 5.85 14.35 16.41 9.4 ...
```

```
#>    ..$ PM25_3 : num [1:1000] 11.17 5.9 20.8 18.95 8.62 ...
#>    ..$ PM25_4 : num [1:1000] 7.56 5.36 14.85 11.54 6.67 ...
#>    ..$ PM25_5 : num [1:1000] 22.71 5.28 10.67 8.23 9.31 ...
#>    ..$ PM25_6 : num [1:1000] 11.4 5.62 9.44 16.92 7.47 ...
#>    ..$ PM25_7 : num [1:1000] 7.56 6.98 16.63 7.9 10.18 ...
#>    ..$ PM25_8 : num [1:1000] 8.74 5.41 7.37 12.55 10.77 ...
#>    ..$ PM25_9 : num [1:1000] 11.03 6.02 13.76 10.69 10.91 ...
#>    ..$ PM25_10: num [1:1000] 7.01 6.83 10 6.38 10.38 ...
#>    ..$ PM25_11: num [1:1000] 8.45 9.88 6.43 7.84 8.11 ...
#>    ..$ PM25_12: num [1:1000] 6.51 8.76 7.74 9.32 10.43 ...
#>    ..$ PM25_13: num [1:1000] 10.21 9.4 9.25 10.92 6.96 ...
#>    ..$ PM25_14: num [1:1000] 6.23 9.04 10.99 6.77 8.7 ...
#>    ..$ PM25_15: num [1:1000] 7.69 9.94 7.29 6.73 10.18 ...
#>    ..$ PM25_16: num [1:1000] 9.8 10.36 6.7 9.97 13.58 ...
#>    ..$ PM25_17: num [1:1000] 8.4 10.87 10.29 7.69 12.29 ...
#>    ..$ PM25_18: num [1:1000] 7.12 7.8 7.17 7.48 14.43 ...
#>    ..$ PM25_19: num [1:1000] 7.26 11.51 7.33 6.51 13.51 ...
#>    ..$ PM25_20: num [1:1000] 8.71 9.42 7.01 11.32 10.4 ...
#>    ..$ PM25_21: num [1:1000] 6.63 7.6 11.68 8.16 9.01 ...
#>    ..$ PM25_22: num [1:1000] 10.48 10.42 7.17 5.55 9.79 ...
#>    ..$ PM25_23: num [1:1000] 9.16 11.35 6.39 12.78 8.78 ...
#>    ..$ PM25_24: num [1:1000] 11.65 8.91 14.66 14.39 12.97 ...
#>    ..$ PM25_25: num [1:1000] 13.86 11.61 11.68 9.42 7.31 ...
#>    ..$ PM25_26: num [1:1000] 6.84 6.57 10.32 9.14 4.9 ...
#>    ..$ PM25_27: num [1:1000] 12.68 7.59 9.3 14.54 8.29 ...
#>    ..$ PM25_28: num [1:1000] 8.83 8.7 15.13 11.79 7.29 ...
#>    ..$ PM25_29: num [1:1000] 9.09 6.27 11.55 11.31 10.24 ...
#>    ..$ PM25_30: num [1:1000] 11.12 8.83 11.69 12.86 6.72 ...
#>    ..$ PM25_31: num [1:1000] 8.34 7.71 11.14 9.23 7.81 ...
#>    ..$ PM25_32: num [1:1000] 7.58 8.8 11.96 14.72 8.03 ...
#>    ..$ PM25_33: num [1:1000] 10.08 7.18 11.98 13.78 7.02 ...
#>    ..$ PM25_34: num [1:1000] 11.88 9.19 14.53 13.28 7.86 ...
#>    ..$ PM25_35: num [1:1000] 7.14 5.94 13.38 8.76 8.23 ...
#>    ..$ PM25_36: num [1:1000] 7 6 7.88 11.14 7.75 ...
#>    ..$ PM25_37: num [1:1000] 7.22 8.13 13.02 19.72 11.41 ...
#>  $ modifier: num [1:1000] 0.141 0.605 0.375 0.703 0.833 ...
#>  $ z       : num [1:1000, 1:3] -1.462 -0.44 0.941 0.969 1.708 ...
```

This data set is a list containing the response ($y), the exposure history ($exposure), the modifier ($modifier), and covariates ($z). Now fit the DLIM using the dlim function:

```
dlim_fit <- dlim(y = ex_data$y,
                 x = ex_data$exposure,
                 modifier = ex_data$modifier,
                 z = ex_data$z,
                 df_m = 10,
                 df_l = 10)
```

Note that the default is to use penalization. We can quickly look at the object by printing it:

```
dlim_fit
#> Object of class dlim
#>
```

```
#> Family: gaussian
#> Link function: identity
#>
#> dlim(y = ex_data$y, x = ex_data$exposure, modifiers = ex_data$modifier,
#>     z = ex_data$z, df_m = 10, df_l = 10)
#> Modifier basis degrees of freedom: 10
#> Exposure time basis degrees of freedom: 10
#>
#> Number of exposure time points: 37
#>
#> Penalization: Yes
#>
#> n = 1000
```

This tells us the GAM was fit using the Gaussian family and identity link function, there are 10 degrees of freedom for both bases, the number of exposure time points is 37, and the model was fit using penalization.

Prediction

To see predicted cumulative or point-wise effects, we can use the `predict()` function. Specify `type="CE"` to obtain cumulative effect estimates, `type="DLF"` to obtain point-wise effect estimates, or `type=c("CE","DLF")` to obtain both. The order does not matter. The following gives cumulative effect estimates for a modifier value of 0.5, along with upper and lower confidence intervals:

```
dlim_pred <- predict(dlim_fit,
                     newdata = 0.5,
                     type="CE")
data.frame(cumul_betas = c(dlim_pred$est_dlim$betas_cumul),
           LB = c(dlim_pred$est_dlim$cumul_LB),
           UB = c(dlim_pred$est_dlim$cumul_UB))
#>   cumul_betas       LB       UB
#> 1    2.521887 2.465761 2.578014
```

The following gives point-wise effect estimates for a modifier value of 0.5, along with upper and lower confidence intervals:

```
dlim_pred <- predict(dlim_fit,
                     newdata = 0.5,
                     type="DLF")
data.frame(betas = c(dlim_pred$est_dlim$betas),
           LB = c(dlim_pred$est_dlim$LB),
           UB = c(dlim_pred$est_dlim$UB))
#>         betas             LB         UB
#> 1  0.015493436 -0.0088212123 0.03980809
#> 2  0.012681762 -0.0038701390 0.02923366
#> 3  0.009452520 -0.0034498292 0.02235487
#> 4  0.006252764 -0.0055033865 0.01800891
#> 5  0.003529548 -0.0090522753 0.01611137
#> 6  0.001729924 -0.0119363763 0.01539622
#> 7  0.001305969 -0.0117704259 0.01438236
#> 8  0.002738391 -0.0086632348 0.01414002
#> 9  0.006518027 -0.0042045510 0.01724061
```

```
#> 10 0.013135728  0.0012408808 0.02503058
#> 11 0.023082344  0.0098801793 0.03628451
#> 12 0.036766674  0.0240577371 0.04947561
#> 13 0.053832923  0.0429503442 0.06471550
#> 14 0.073509141  0.0636647488 0.08335353
#> 15 0.095019208  0.0842061010 0.10583231
#> 16 0.117587005  0.1053237412 0.12985027
#> 17 0.140398284  0.1282795013 0.15251707
#> 18 0.162011780  0.1515156855 0.17250787
#> 19 0.180472918  0.1710107331 0.18993510
#> 20 0.193812020  0.1833817000 0.20424234
#> 21 0.200059408  0.1879785198 0.21214030
#> 22 0.197301455  0.1849772032 0.20962571
#> 23 0.185529686  0.1745899300 0.19646944
#> 24 0.167062793  0.1572475206 0.17687807
#> 25 0.144360981  0.1338786290 0.15484333
#> 26 0.119884457  0.1078931310 0.13187578
#> 27 0.096085930  0.0837886022 0.10838326
#> 28 0.074669984  0.0637996782 0.08554029
#> 29 0.055966672  0.0463572346 0.06557611
#> 30 0.040158546  0.0298310819 0.05048601
#> 31 0.027428157  0.0152862404 0.03957007
#> 32 0.017957869  0.0049832833 0.03093246
#> 33 0.011768375 -0.0005820517 0.02411880
#> 34 0.008423399 -0.0036475010 0.02049430
#> 35 0.007406503 -0.0059269186 0.02073992
#> 36 0.008201245 -0.0082854634 0.02468795
#> 37 0.010291185 -0.0133044965 0.03388687
```
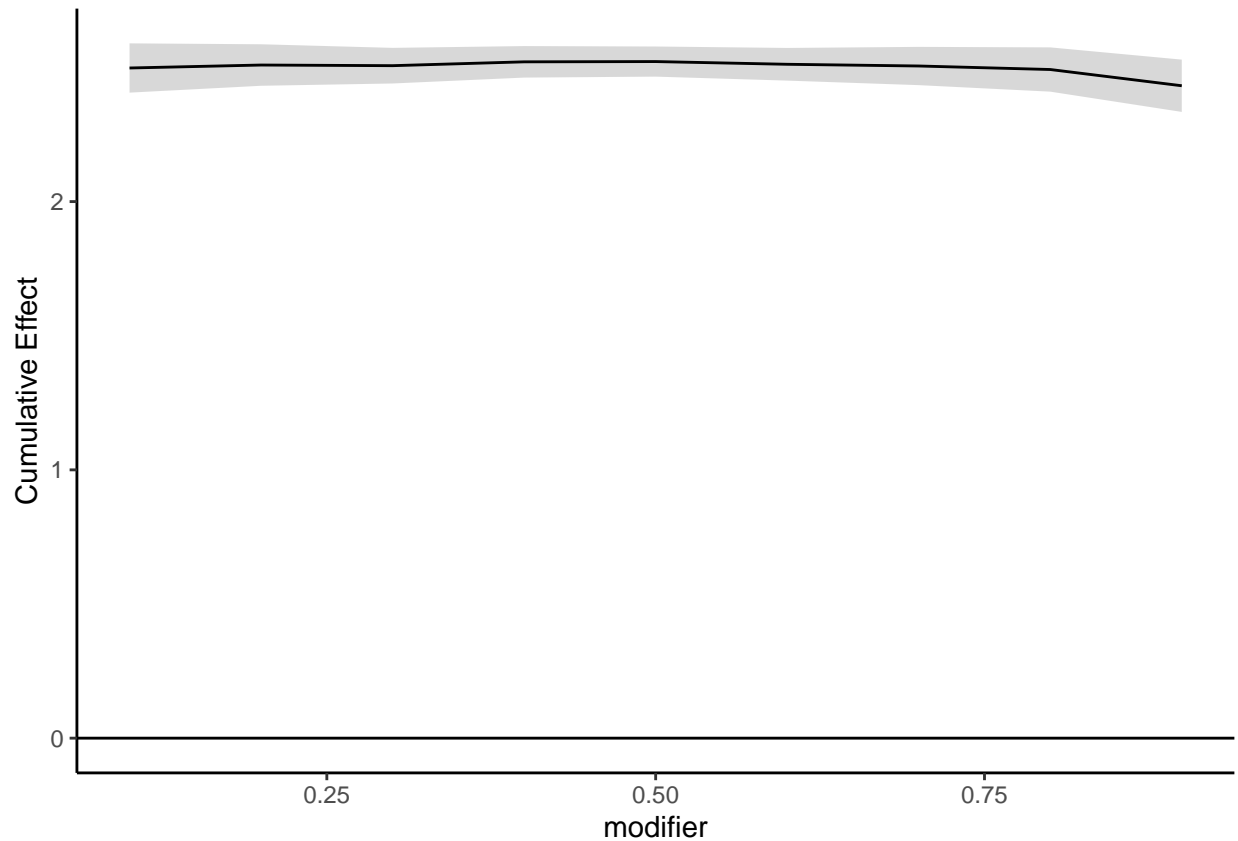
Plotting

Standard plotting functions

We can also create plots for the cumulative effects and point-wise effects. The following plots the estimated cumulative effects over a grid of modifier values:

```
plot_cumulative(new_modifiers = seq(0.1,0.9,0.1),
                mod_fit = dlim_fit,
                mod_name = "modifier")
```

There are two ways to look at estimated point-wise effects: by modifier or by time. To create a grid of estimated point-wise effect plots for a select number of time points, specify `plot_by = time` and provide select time points to `time_pts`. The following plots estimated point-wise effects across a grid of modifiers isolated for weeks 10, 20, and 30:

```
plot_DLF(new_modifiers = seq(0.1,0.9,0.1),
         mod_fit = dlim_fit,
         mod_name = "modifier",
         plot_by = "time",
         time_pts = c(10,20,30))
```
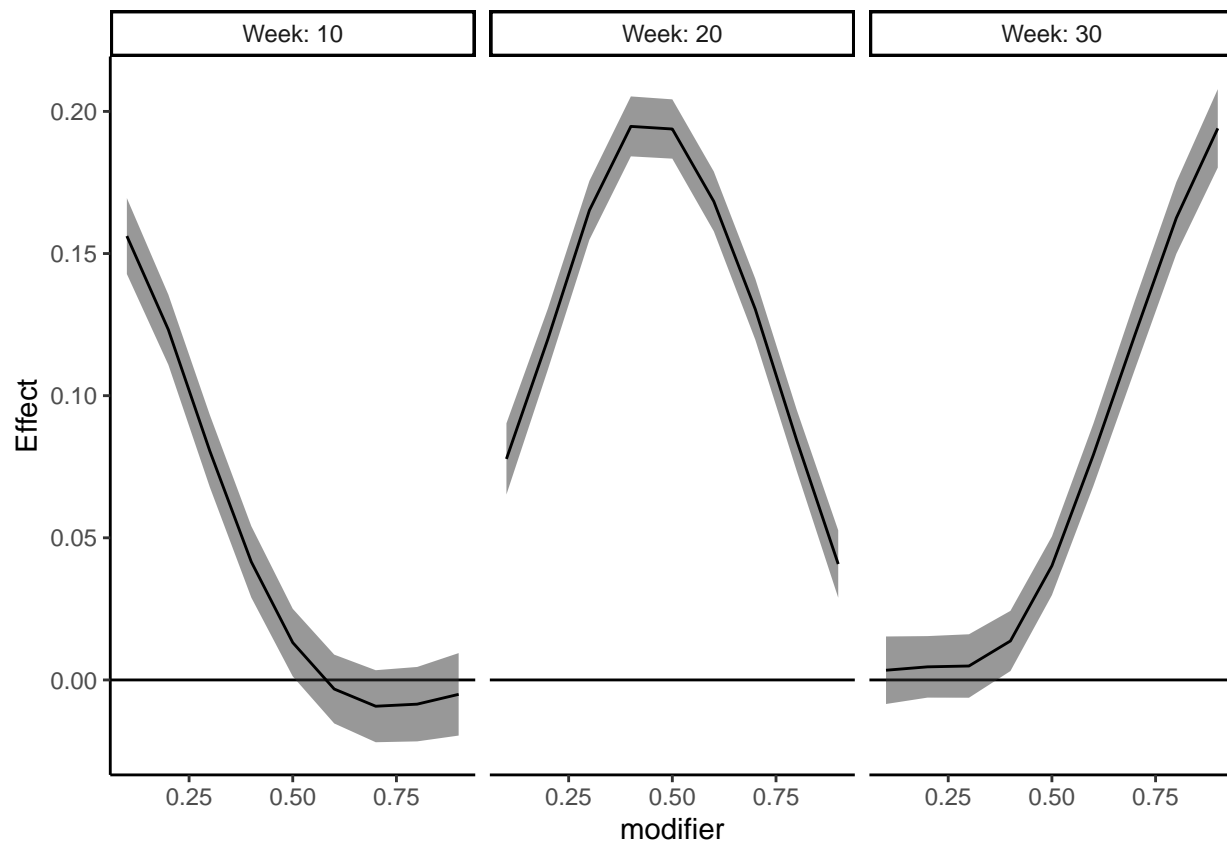
To create a grid of estimated point-wise effect plots for a select number of modifier values, specify `plot_by = modifier` and provide select modifier values to `new_modifiers`. The following plots estimated point-wise effects across all time points isolated for modifier values 0.25, 0.5, and 0.75.

```
plot_DLF(new_modifiers = c(0.25, 0.5, 0.75),
         mod_fit = dlim_fit,
         mod_name = "modifier",
         plot_by = "modifier")
```
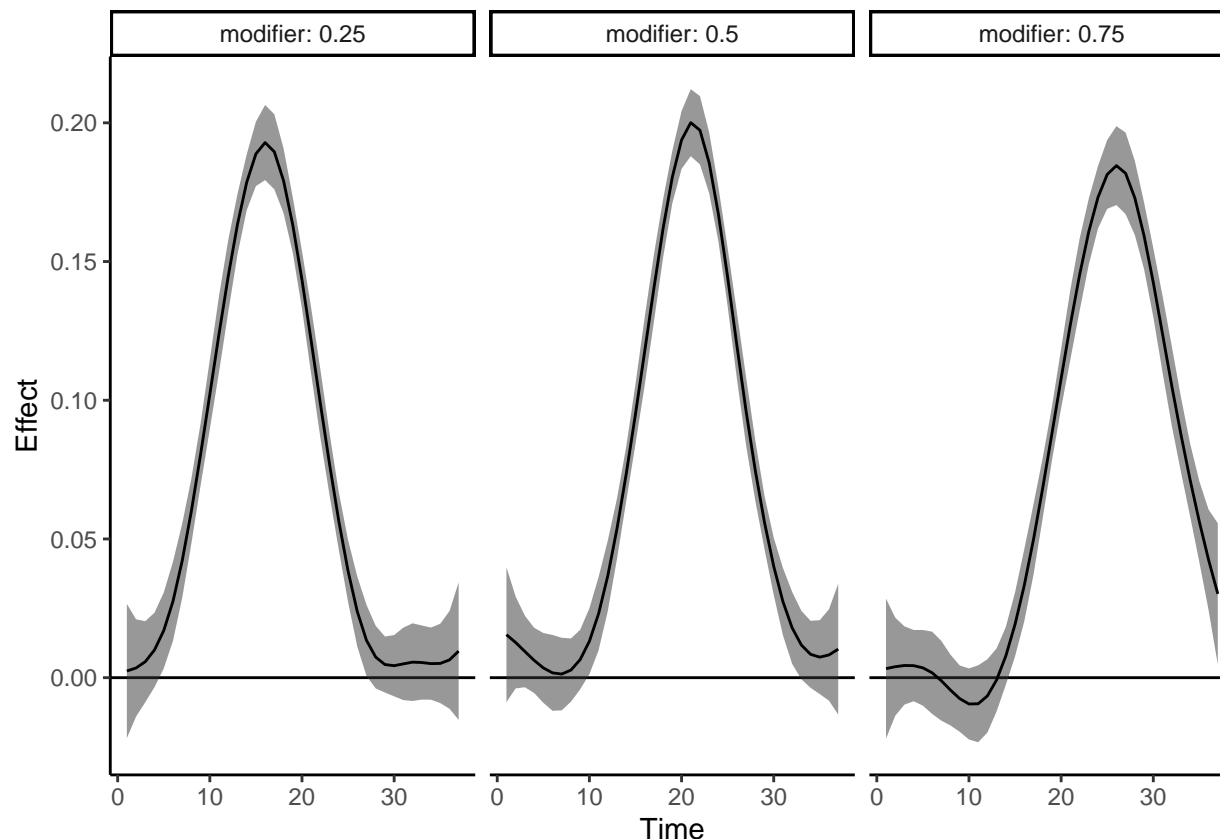
Custom plotting examples

You can use the output from the `predict` function to create your own custom plots. To create a custom cumulative effect plot, specify a range of modifier value through `newdata` in the `predict` function, and then extract the cumulative effect estimates (`dlim_pred$est_dlim$betas_cumul`), and the upper (`dlim_pred$est_dlim$cumul_UB`) and lower `dlim_pred$est_dlim$cumul_LB` bounds for the cumulative effects. Combine these along with the modifiers into a data frame and plot using `ggplot` or `plot`.

```
#predict
dlim_pred <- predict(dlim_fit,
                     newdata = seq(0.1, 0.9, 0.1))
#> Returning fitted values is in progress.

#create data frame for plotting
dlim_cumul_df <- data.frame(Estimate = c(dlim_pred$est_dlim$betas_cumul),
                            LB = c(dlim_pred$est_dlim$cumul_LB),
                            UB = c(dlim_pred$est_dlim$cumul_UB),
                            Modifier = c(dlim_pred$est_dlim$modifiers))

#plotting
ggplot(dlim_cumul_df, aes(x = Modifier, y = Estimate)) +
    geom_point(color = "blue") +
    geom_errorbar(aes(ymin=LB, ymax=UB)) +
    geom_hline(yintercept = 0,  color = "black", size=1) +
    xlab("Modifier") +
```
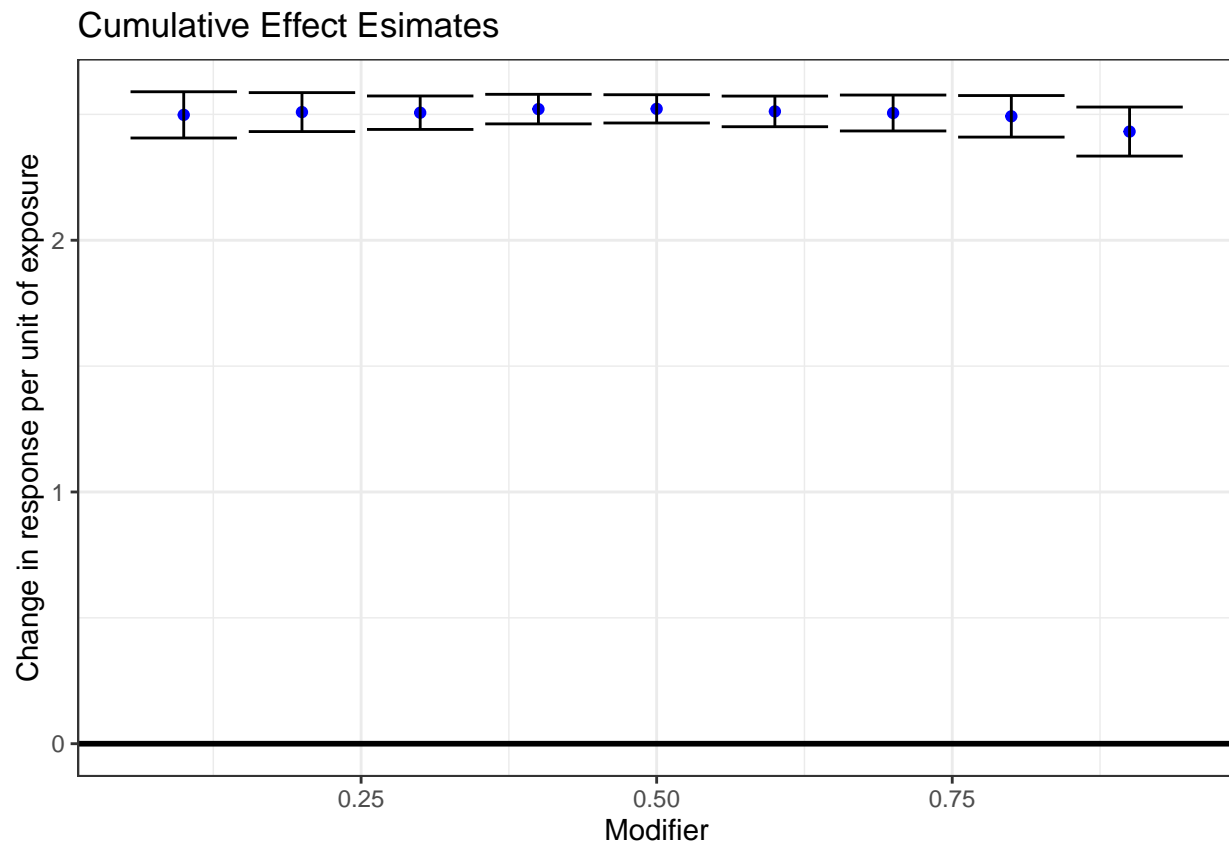
```
    ylab("Change in response per unit of exposure") +
    ggtitle("Cumulative Effect Esimates") +
    theme_bw()
#> Warning: Using `size` aesthetic for lines was deprecated in ggplot2 3.4.0.
#> i Please use `linewidth` instead.
#> This warning is displayed once every 8 hours.
#> Call `lifecycle::last_lifecycle_warnings()` to see where this warning was
#> generated.
```

Cumulative Effect Esimates

To make a custom plot of the exposure-time-response functions for specific modifier values, you can follow a similar approach. Specify the modifiers you want to use with `newdata` in the `predict` function and set `type = "DLF"` to obtain point-wise effect estimates. Then extract the point-wise effect estimates (`dlim_pred$est_dlim$betas`), and the upper (`dlim_pred$est_dlim$UB`) and lower (`dlim_pred$est_dlim$LB`) bounds. Note the use of the transpose function to make sure they are vectorized in proper order. The dimensions of each of these matrices is the number of modifier values specified by the number of exposure-time points.

```
#predict
new_mods <- c(0.25, 0.5, 0.75)
dlim_pred <- predict(dlim_fit,
                     newdata = c(0.25, 0.5, 0.75),
                     type = "DLF")

#create data frame for plotting
dlim_pred_df <- data.frame(Estimate = c(t(dlim_pred$est_dlim$betas)),
                           LB = c(t(dlim_pred$est_dlim$LB)),
```
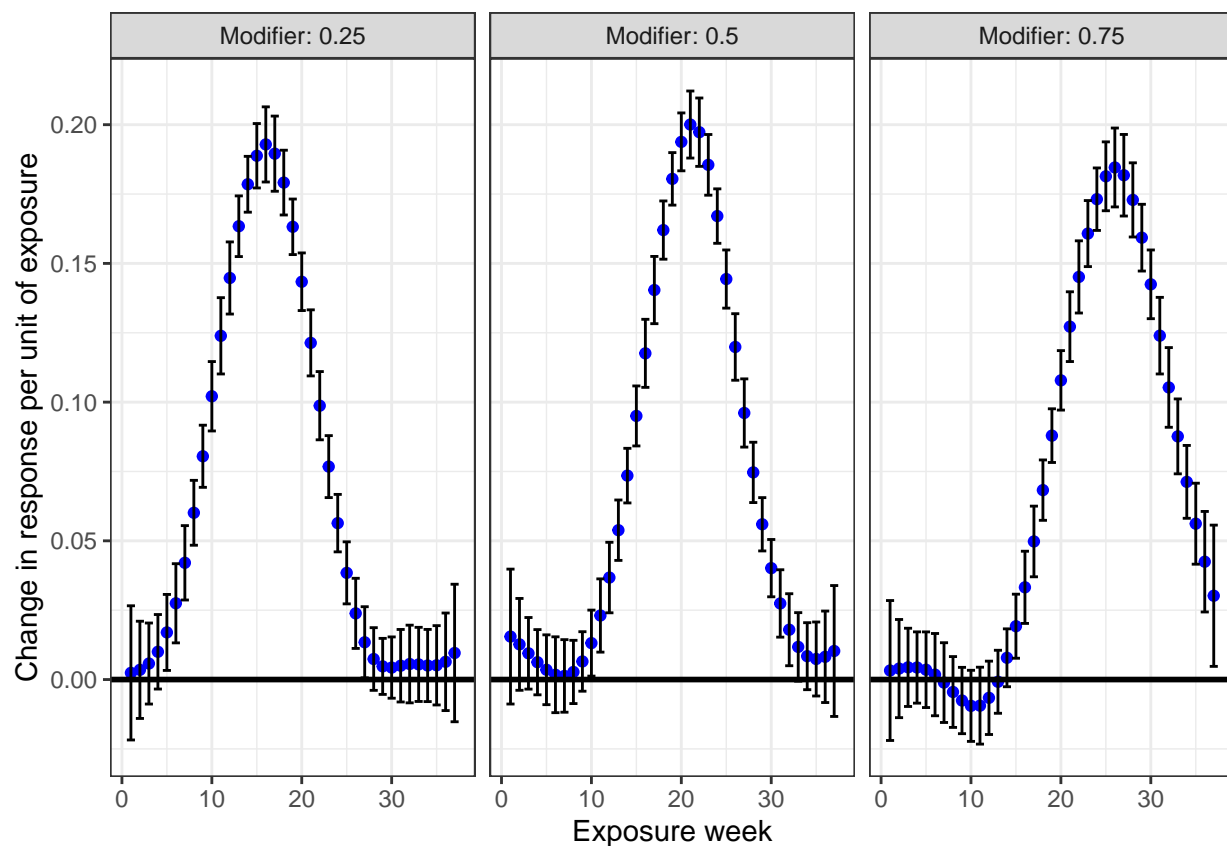
```
                          UB = c(t(dlim_pred$est_dlim$UB)),
                          Week = rep(1:37,length(new_mods)),
                          Modifier = rep(new_mods, each = 37))

#plotting
ggplot(dlim_pred_df, aes(x = Week, y = Estimate)) +
    geom_point(color = "blue") +
    geom_errorbar(aes(ymin=LB, ymax=UB)) +
    geom_hline(yintercept = 0,  color = "black", size=1) +
    facet_grid(cols = vars(Modifier), labeller = "label_both") +
    xlab("Exposure week") +
    ylab("Change in response per unit of exposure") +
    theme_bw()
```


Model Comparison

We can compare this model to a standard DLM using the `model_comparison` function. The full model is the `dlim_fit` model object, and the null model by default is `"none"`, a DLM with no interaction (standard DLM). Then, specify the exposure used to create `dlim_fit` and the number of bootstrap samples, `B = 5` (we recommend using at least 1000 bootstrap samples, but use 5 to illustrate quickly). The function returns the decision to reject or fail to reject the null model based on the default confidence level `conf.level` of 0.95.

```
model_comparison(fit = dlim_fit,
                 null = "none",
                 x = exposure,
                 B = 5)
#>      95%
#> "reject"
```

There are 6 different types of model comparisons this function supports:

1. DLIM with non-linear interaction v. DLIM with quadratic interaction (`attr(fit, "model_type")` == `"nonlinear"` and `null = "quadratic"`)

2. DLIM with non-linear interaction v. DLIM with linear interaction (`attr(fit, "model_type")` == `"nonlinear"` and `null = "linear"`)

3. DLIM with non-linear interaction v. standard DLM without interaction (`attr(fit, "model_type")` == `"nonlinear"` and `null = "none"`)

4. DLIM with quadratic interaction v. DLIM with linear interaction (`attr(fit, "model_type")` == `"quadratic"` and `null = "linear"`)

5. DLIM with quadratic interaction v. standard DLM without interaction (`attr(fit, "model_type")` == `"quadratic"` and `null = "none"`)

6. DLIM with linear interaction v. standard DLM without interaction (`attr(fit, "model_type")` == `"linear"` and `null = "none"`)

Bibliography

Demateis, D., Keller, K. P., Rojas-Rueda, D., Kioumourtzoglou, M.-A., & Wilson, A. (2024). Penalized distributed lag interaction model: Air pollution, birth weight, and neighborhood vulnerability. Environmetrics, e2843. https://doi.org/10.1002/env.2843