Distributed lag non-linear models in R: the package dlnm

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dlnm version 1.1.1 , 2009-11-03

Contents

[1]This work was supported by the Medical Research Council (UK) through the Research Grant RES-G0707030.

1 Preamble

This document is included as a vignette (a LaTeX document created using the R function `Sweave()`) of the package dlnm. It is automatically dowloaded together with the package and can be accessed through R typing *`vignette("dlnmOverview")`*, or otherwise directly in the path `library/dlnm/doc` within the R folder. A file named `dlnmOverview.R` containing the R pieces of code (*chunks*) illustrated here can be found in the same folder and run to check the results. Type *`citation("dlnm")`* in R to cite this package. A list of changes included in the current and previous versions can be found typing *`file.show(system.file("ChangeLog", package = "dlnm"))`*.

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2 Introduction

The R package dlnm provides some facilities to run *distributed lag non-linear models* (DLNM's), a modelling framework to describe simultaneously non-linear and delayed effects between predictors and an outcome in time-series data.

The aim of this document is to provide an extended overview of the capabilities of the package, including an detailed summary of the functions included here, with some examples of application to real data. Although these examples refer to the health effects of air pollution and temperature, the purpose of package is fairly general, and it can be used to specify DLNM's in order to investigate the relationship between series of any predictors and outcomes.

The remainder of Section 2 provides some information on the installation of the package dlnm and on the data used throughout this document. The family DLNM's is introduced in Section 3, while the R functions used to specify them are described in Section 4. Three different examples are illustrated in Section 5: users mainly interested in the application of DLNM's can skip the previous sections and start with these examples.

We state beforehand that the goal of the examples included in this document is to describe the functionalities of the package, and that the results should not be used to infer some conclusions on the causal associations of the relationships considered there.

2.1 Installing the package dlnm

The dlnm package is installed in the standard way for CRAN packages, for example using the `install.packages()` function or directly through the menu in R (from version 2.9.0 onwards), clicking on *Packages* and then on *Install package(s)...*. The package can be alternatively installed using the .zip file containing the binaries, via *Packages* and then *Install package(s) from local zip files...*.

The functionalities of dlnm depend on other packages whose commands are used to specify the dlnm functions. This hierarchy is ruled by the field *Imports* of the file `description` included in the package. The functions are imported from the packages splines (functions `ns()` and `bs()`) and tsModel (function `Lag()`). While splines is present in the basic installation of R, the package tsModel is automatically downloaded if dlnm is installed through R using the CRAN, but must be independently installed if a .zip file is used.

The package dlnm is assumed to be present in the R library and loaded in this session. If not, type:

```
> library(dlnm)
```

2.2 Data

Until the version 0.4.1, the package dlnm did not contain any data, and used the datasets stored in the package NMMAPSlite.

Now the dlnm package contains its own dataset chicagoNMMAPS, with daily mortality (all causes, CVD, respiratory), weather (temperature, dew point temperature, relative humidity) and pollution data (PM10 and ozone) for Chicago in the period 1987-2000. The data were assembled from publicly available data sources as part of the National Morbidity, Mortality, and Air Pollution Study (NMMAPS) sponsored by the Health Effects Institute [13, 12]. They are downloadable from the Internet-based Health and Air Pollution Surveillance System (iHAPSS) website (http://www.ihapss.jhsph.edu) or through the packages NMMAPSdata or NMMAPSlite. See *?chicagoNMMAPS* for additional information on the variables included.

The database is loaded in the R session by:

```
> data(chicagoNMMAPS)
```

3 Distributed lag non-linear models (DLNM's)

The aim of this Section is to provide a summary on the framework of DLNM's. A detailed overview of this family of models have already been published elsewhere [3, 8].

3.1 The issue

The main purpose of a statistical regression model is to define and then estimate the effect of a regressor on an outcome. A first problem arises when the relationship between them is non-linear: several possible solutions have been proposed, and many of them involve a manipulation of the original variable in order to specify one or more new predictors which must explain, globally, the shape of the dependency: a simple example is the inclusion of a quadratic term in the model.

A further complexity occurs when the effect of a specific occurrence of the predictor is not limited to the period when it is observed, but is *delayed* in time. In this case, more complex models are required to specify the dependency, taking into account the inclusion of the additional time dimension.

3.2 The concept of basis

Several different methods have been adopted to specify non-linear effects in a regression models. A simple solution is to generate strata variables, applying specific cut-off points along the range of the predictor in order to define specific intervals, and then specifying new variables through a dummy parameterization.

Other types of manipulations of the original variable are applied when there are specific assumptions on the shape of the relationship, for example when the effect is likely to exist and be linear only above or below a specific threshold (*hockey-stick* model). An extension of this model assumes two distinct linear effects below a first threshold and above a second threshold, with a null effect in between them.

An alternative to the strata or threshold approaches is to include in the model some terms allowing a true non-linear relationship, describing a smoothed curve between the predictor and the outcome. The traditional methods include a quadratic term or higher degree polynomials. Recently, spline functions have been favoured, especially through a natural cubic parameterization.

A generalization may be provided assuming that all the approaches above imply the choice of a *basis*, defined as a *space of functions* used to define the relationship [18]. The choice of the basis defines the related *basis functions*, completely known transformations of the original predictor generating a new set of transformed variables, defined *basis variables*. Independently from the basis chosen, the final result will be a matrix of transformed variables which can be included in the design matrix of a model in order to estimate the related parameters. The choice of different bases leads to the specification of different matrices, but the mechanism is common.

3.3 Delayed effect: DLM's

In the specific context of time series analysis, given the ordered series of the predictor values, a delayed (or lagged) effect is present when the outcome in a specific day is influenced by the level of the predictor in the days before, up to a maximum lag. Therefore, the presence of delayed effects requires to take into account the *time dimension* of the relationship, specifying the additional *virtual* dimension of the lags.

A very simple model to deal with delayed effects considers the moving average of the predictor up to a certain lag, specifying a transformed predictor which is the average of the values in that specific lag period. Although simple, this model is limited if the purpose is to assess the temporal structure of the effects.

These limitations have been addressed using a more elegant approach based on distributed lag models (DLM's). The main advantage of this method is the possibility to depict a detailed description of the time-course of the relationship. Originally developed in econometrics [1], this method has recently been used to quantify the health effect in studies on environmental factors [20, 15, 17, 5].

In the basic formulation, a DLM is fitted including a parameter for each lagged predictor occurrence. An estimate of the overall effect is given by the sum of the single lag effects upon the whole lag period considered [14, 9].

This *unconstrained* version of DLM does not require any assumption on the shape of the effect along lags, and consequently on the relationship between parameters. In order to define a more parsimonious model, it is possible to specify some assumptions on the shape of the distributed effect, applying some constraint. The simplest solution is to group the lags in different strata [17, 10], while a more complex option is to force the curve along lags to follow a specific smooth function, for example polynomials [19, 16, 4] or splines [20].

Following the general approach used in Section 3.2, it may be shown [8] that all the different DLM's above can be described by the same equation, where different models are specified through different basis functions to be applied to the virtual vector of lags, building a new basis matrix. Again, the choice of different bases generates different matrices, but the mechanism is general.

3.4 The extension to DLNM's

A general approach to specify non-linear but un-lagged effects has been introduced in Section 3.2, while the methods to define distributed lag functions for simple linear effects have been presented in Section 3.3. An obvious extensions is to combine these approaches to define distributed lag non-linear models (DLNM's), a family of models which can deal at the same time with non-linear and delayed effects [3, 8].

The different issues of non-linearity and delayed effects share a common feature: in both cases the solution is to choose a basis to describe the shape of the relationship in the relative dimension. This step leads to the concept of *cross-basis*: following the idea of basis in 3.2, a cross-basis can be imagined as a bi-dimensional space of functions describing on the same time the shape of the relationship and the distributed lag effects. The algebraic notation to define the cross-basis and then the DLNM can be quite complex, involving tensor products of 3-dimensional arrays, and has been presented elsewhere [8]. Nonetheless, the basic concept is straightforward: choosing a cross-basis amounts to choosing two independent set of basis functions, which will be combined to generate the specific cross-basis functions. The DLM's described in 3.3 can be considered as special cases of DLNM's with a simple linear function in the dimension of the predictor.

The result of a DLNM can be interpreted building a grid of predictions for each lag and for suitable values of the predictor, using three dimensional plots to provide an overall picture of the effects varying along the two dimensions. In addition, it is possible to compute the effects for single predictor levels or lags, simply cutting a "slice" of the grid along specific values of predictor or lags, respectively. Finally, an estimate of the overall effect can be computed by summing all the contributions at different lags. The effects are usually reported versus a reference value of the predictor, centering the basis functions for this space to their corresponding transformed values [6].

The choice of the two set of basis functions for each space is perfectly independent, and should be based on a-priori assumptions or on a compromise between complexity and generalizability. Linear, threshold, strata, polynomial or splines functions can be used to define the relationship along the space of predictor, while unconstrained, strata, polynomial or splines functions can be applied to specify the shape along lags.

The package dlnm provides a function named `crossbasis()` to specify the cross-basis matrix, given the choices on the two bases among the options listed above, and two other functions `crosspred()` and `crossplot()` to predict and plot the estimated effects, respectively.

4 The functions in the package dlnm

The functions included in the package can be used to complete all the steps required to specify and interpret a DLNM.

First, the internal functions `mkbasis()` and `mklagbasis()` are called in order to build the basis matrices for the dimension of the predictor and lags, respectively. In concrete terms, they apply a transformation to the vector of predictor and to the vector of lags, and stored the transformed variables in two matrix objects. Details on the basis specification are given in Section 3. These two internal commands are called directly by `crossbasis()`, and they are not meant to be run by the users.

The main function in the package dlnm is `crossbasis()`. It calls the internal functions `mkbasis()` and `mklagbasis()` and combines the two basis matrices in order to create the cross-basis matrix which specifies the dependency simultaneously in the two dimensions. The function `summary.crossbasis()` provides a summary of the choices made for the two bases and the final cross-basis. The cross-basis matrix should be included in the model formula of default model commands to estimate the parameters defining the shape of the effects along the space of the predictor and along lags. The package dlnm has been tested with the model function `glm()`; the accuracy of the results obtained with other commands is not guaranteed and should be carefully checked.

The function `crosspred()` generates the predicted effects for a set of values of the original predictor, given the applied cross-basis functions and the parameters estimated by the model. It stores them in matrices with specific effects for each combination of predictor values and lags, and in vectors of overall effects (summed up along lags).

Finally, the function `crossplot()` provides some options to visualize the predicted effects.

See the related help pages (for example *`help(crossbasis)`* or *`?crossbasis`*) for the details on the usage and the arguments of these functions.

5 Some examples

This Section provides some examples of the use of the various functions included in the dlnm package, described in Section 4.

First, some simple examples of the internal functions `mkbasis()` and `mklagbasis()` are showed in Section 5.1. Although these commands are not meant to be performed directly by the user, but are commonly called through `crossbasis()`, these codes can shine a light on the process to build the basis functions for the two dimensions (predictor and lags), and clarify the meaning of the arguments of the function `crossbasis()`.

Then, 3 different examples of the application of DLNM's are illustrated in the Sections 5.2-5.4, using the NMMAPS dataset for the city of Chicago in the period 1987-2000 described in Section 2.2. These different cases cover most of the functionalities of the package, providing a detailed overview of its capabilities and a basis to perform analyses on this dataset or on other data sources.

The models included in the examples do not contain other important confounders which are commonly accounted for in the time series analysis of the effect of environmental factors [7, 11, 2]. However, as already stated above, the examples are included only with the aim to illustrate the use of the functions in the dlnm package, and the results should not be considered as scientific evidences. In spite of this, these confouders can be easily added to the model formula in order to perform a proper statistical analysis, without any changes to the specification of the dlnm functions.

5.1 Examples for `mkbasis()` and `mklagbasis()`

As a first step, we provide an example of the use of the function `mkbasis()`. We build a basis matrix applying the selected basis functions to the vector of integers going form 1 to 5. We leave many of the arguments at their default values, apart from the selection of the degrees of freedom `df`.

```
> basis.var <- mkbasis(1:5, knots=3)
> basis.var

$basis
             b1          b2
[1,] -0.56626284  0.21084190
[2,] -0.20921622 -0.00635585
[3,]  0.00000000  0.00000000
[4,] -0.03716777  0.37894518
[5,] -0.22216593  0.98144395

$type
[1] "ns"

$df
[1] 2

$knots
[1] 3

$bound
[1] 1 5

$int
[1] FALSE

$cen
[1] TRUE

$cenvalue
[1] 3
```

The chosen basis is a natural cubic B-splines (default `type="ns"`) with the 1 knots and `df=2` (`df` is equal to `length(knots)+1+int` for `type="ns"`). Apart from the fact that the basis variables are centered at `cenvalue=3` (the mean of the predictor values, the default for this argument), the same results could be obtained by the command *`ns(1:5,knots=3)`*. The basis matrix is stored in the object `basis.var$basis`, while the arguments specifying it are included as other objects in the list, and can be called directly (for example, try *`basis.var$knots`*).

Alternative choices may be specified through the following code (results not shown, the user can try to run the commands):

```
> mkbasis(1:5, type="bs", df=4, degree=2)
> mkbasis(1:5, type="lin", cenvalue=4)
```

In the first case the result is a quadratic spline where the number and location of `knots` are chose automatically, and fixed to 2 (`df` is `length(knots)+degree+int` for this `type`) and at equally spaced quantiles, respectively. The second line returns a simple linear function, where the only transformation is the centering at the value of 4.

The function `mklagbasis()` calls `mkbasis()` to create a basis matrix for the space of the lag. The basis functions are applied to the vector `0:maxlag` expressly created by the function. These are two examples of application:

```
> mklagbasis(maxlag=5, type="poly", degree=3)

$basis
     b1 b2 b3  b4
lag0  1  0  0   0
lag1  1  1  1   1
lag2  1  2  4   8
lag3  1  3  9  27
lag4  1  4 16  64
lag5  1  5 25 125

$type
[1] "poly"

$df
[1] 4

$degree
[1] 3

$int
[1] TRUE

$maxlag
[1] 5

> mklagbasis(maxlag=5, type="integer")

$basis
     b1 b2 b3 b4 b5 b6
lag0  1  0  0  0  0  0
lag1  0  1  0  0  0  0
lag2  0  0  1  0  0  0
lag3  0  0  0  1  0  0
lag4  0  0  0  0  1  0
```

```
lag5  0  0  0  0  0  1

$type
[1] "integer"

$df
[1] 6

$int
[1] TRUE

$maxlag
[1] 5
```

The first line specifies a 3$^{\text{rd}}$ degree polynomial. Differently from the bases for the space of the predictor build above, this matrix contains an intercept (`int=TRUE` by default), in this case a vector of 1's (see *?crossbasis*), and it is never centered. `df` is equal to the degree of the polynomial plus 1 when an intercept is included. In this case, for a polynomial basis, the argument `knots` is not included. The second example refers to an specific transformation in the space of lags in order to define unconstrained distributed lag effects (see *?crossbasis*), simply returning an identity matrix.

Other choices may consider a threshold parameterization, with the following code (results not shown):

```
> mkbasis(1:5, type="dthr", knots=c(2,3))
> mkbasis(1:5, type="hthr", knots=3)
> mkbasis(1:5, type="hthr", knots=c(2,3))
```

In the first example, the result is a double threshold basis which can be applied to describe linear effects below 2 and above 3, with a null effect in between them. In the second case, the choice is for a simple threshold with a linear effect above 3. In the last example, a piecewise linear basis is returned, which can describe a relationship with a first threshold at 2 and then an additional change in slope at 3.

A basis matrix of `type="strata"` with and without intercept is created by (results not shown):

```
> mklagbasis(maxlag=10, type="strata", knots=c(4,7))
> mklagbasis(maxlag=10, type="strata", knots=c(4,7), int=FALSE)
```

In this case, the intercept is represented by the dummy variable for the first stratum (see *?crossbasis*). The values in `knots` specify the cut-off point for the strata, and represent the lower boundaries for the right-open intervals.

The effect of centering is illustrated below (results not shown):

```
> mkbasis(0:10, type="poly", degree=3)
> mkbasis(0:10, type="poly", degree=3, cen=FALSE)
```

Each basis function is centered on the relative transformation of `cenvalue`, which is placed at the mean of the predictor values by default [6].

5.2 Example 1: a simple DLM

The dataset used in the next examples has already been loaded in the R session in Section 2.2.

In this first example, we specify a simple DLM, assessing the effect of PM_{10} on overall mortality, while adjusting for the effect of temperature. In order to do so, we first build two cross-basis matrices for the two predictors, and then include them in a model formula of the command `glm()`. The effect of PM_{10} is assumed as linear in the dimension of the predictor, so, from this point of view, we can define this as a simple DLM even if it estimates also the distributed lag function for temperature, which is included as a non-linear term.

First, we run `crossbasis()` to build the two cross-basis matrices, saving them in two objects. The names of the two objects must be different in order to predict the effects separately for each of them (see *?crosspred*). This is the code:

```
> basis.pm <- crossbasis(chicagoNMMAPS$pm10, vartype="lin", lagtype="poly",
+   lagdegree=4,cen=FALSE,maxlag=15)
> basis.temp <- crossbasis(chicagoNMMAPS$temp, vardf=5, lagtype="strata",
+   lagknots=1, cenvalue=21, maxlag=3)
```

The function `crossbasis()` calls the two internal functions `mkbasis()` and `mklagbasis()` to build the basis matrices. It passes the arguments with stub `var-` to the former, in order to specify the basis functions for the predictor (in this case `chicagoNMMAPS$pm10` and `chicagoNMMAPS$temp`), and the arguments with stub `lag-` to the latter, specifying the basis functions for the expressly created vector `0:maxlag`. Then it combines the two basis matrices to create the final cross-basis variables included in the objects of class *"crossbasis"* (`basis.pm` and `basis.temp`).

In this case, we assume that the effect of PM_{10} is linear (`vartype="lin"`), while we model the relationship with temperature through a natural cubic spline with 5 degrees of freedom (`vartype="ns"`, chosen by default). In this space, the internal knots (if not provided) are located by default at equally spaced quantiles, while the boundary knots are located at the range of the observed values, so we need to specify only `vardf`. We did not center PM_{10}, in order to describe the effect versus a reference value of 0 μgr/m^3 (the same results could be reached setting `cen=TRUE` and `cenvalue=0`). The reference value for temperature is set to 21°C.

The basis for the space of the lags is chosen through the same arguments but with stub `lag-`. We specify the lagged effect of PM_{10} up to 15 days of lag with a 4^{th} degree polynomial function (setting `lagdegree=4`). The delayed effect of temperature are defined by two lag strata (0 and 1-3), assuming the effects as constant within each stratum. The argument `varknots=1` define the lower boundary of the second interval.

An overview of the specifications for the two cross-bases and bases is provided by the function `summary.crossbasis`, which calls the attributes of the `crossbasis` object:

```
> summary(basis.pm)
```

```
CROSSBASIS FUNCTIONS
Observations: 5114
Range: -3.049835 , 356.1768
```

```
Total df: 5
maxlag: 15

BASIS FOR VAR:
type: lin
df: 1

BASIS FOR LAG:
type: poly with degree 4
df: 5
with intercept
```

Now the two crossbasis objects can be included in a model formula in order to fit the DLM. In this case we model the effect assuming an overdispersed Poisson distribution:

```
> model <- glm(death ~  basis.pm + basis.temp, family=quasipoisson(), chicagoNMMAPS)
```

The effects of specific levels of PM_{10} on overall mortality, predicted by the model above, can be computed by the function `crosspred()` and saved in an object with the same class:

```
> pred.pm <- crosspred(basis.pm, model,at=0:20)
```

The argument `at=0:20` states that the prediction must be computed for each integer value from 0 to 20 μgr/m^3. Now that the predicted effects have been stored in `pred.pm`, they can be plot by the function `crossplot()`. The first plot in Figure 1a summarizes the effect along lags of a 10-unit increases in PM_{10}, and it is created by:

```
> crossplot(pred.pm, "slices", var=10,
+   title="Effect of a 10-unit increase in PM10 along lags")
```

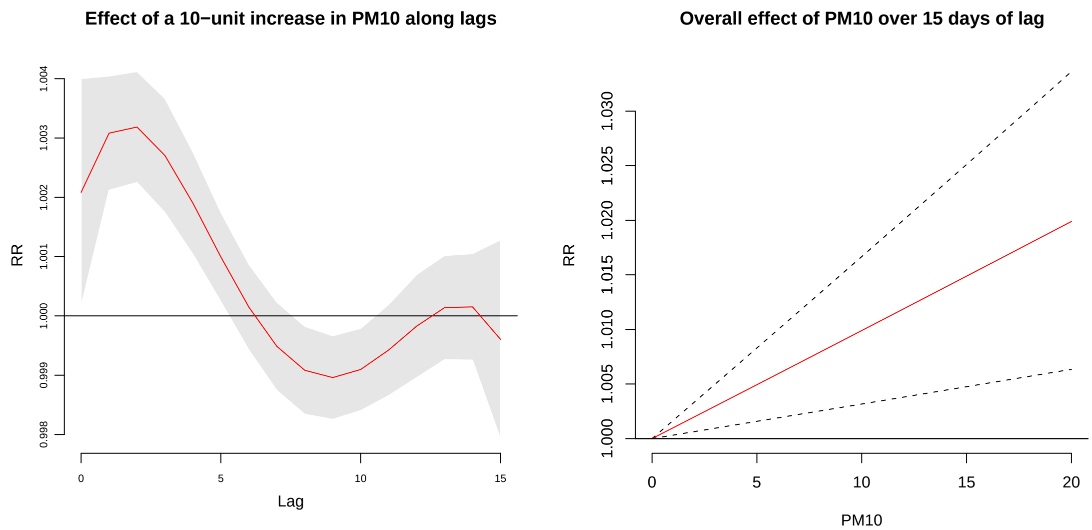
The argument `"slices"` defines that we want to graph the relationship at specific values of the two dimensions (predictor and lag). With `var=10` we specify this relationship along lags for a specific value of PM_{10}, i.e. 10 μgr/m^3. This effect is related to the reference value of 0 μgr/m^3, giving the effect for a 10-unit increase.

Then, we can compute the overall effect for a 10-unit increase in PM_{10} over 15 days of lag (i.e. summing all the effects up to the maximum lag), together with its 95% confidence intervals. These results are stored in the objects `allRRfit`, `allRRhigh` and `allRRlow` included in `pred.pm`, and can be extracted by:

```
> pred.pm$allRRfit["10"]

      10
1.009897

> cbind(pred.pm$allRRlow, pred.pm$allRRhigh)["10",]
```

Figure 1

(a) (b)




```
[1] 1.003167 1.016672
```

The overall effects for the selected range of PM_{10} versus 0 $\mu gr/m^3$ can be then plotted using the argument `type="overall"` in the function `crossplot()`. The argument `ci="lines"` sets a different representation of the confidence intervals. The plot (Figure 1b) is obtained by:

```
> crossplot(pred.pm, "overall", label="PM10", ci="lines",
+   title="Overall effect of PM10 over 15 days of lag")
```

5.3 Example 2: a threshold parameterization

The purpose of the second example is to illustrate the use of the threshold parameterization. We assess the effect of ozone and temperature on overall mortality up to 5 and 15 days of lag, respectively, using the same steps already seen in Section 5.2.

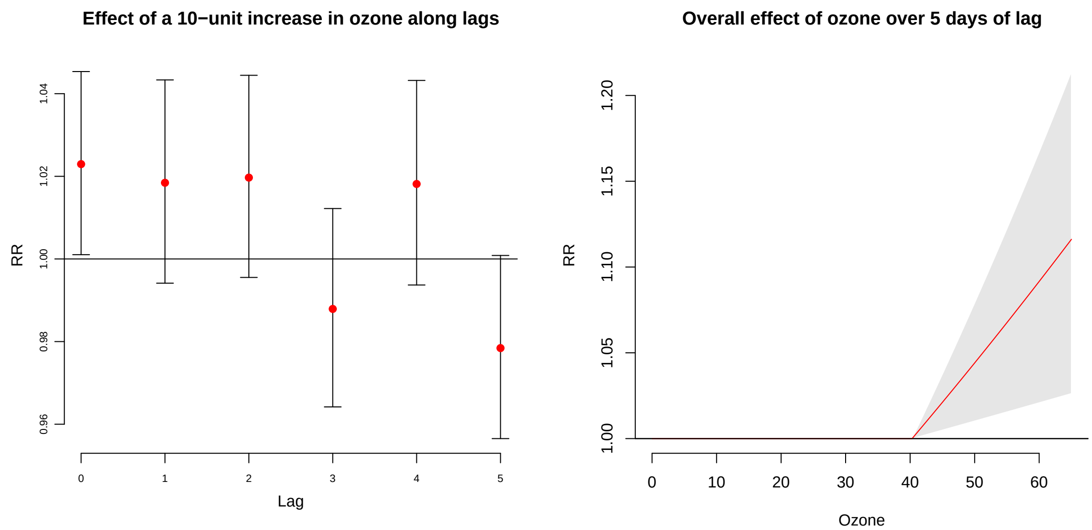
Again, we first create the cross-basis matrices:

```
> basis.o3 <- crossbasis(chicagoNMMAPS$o3, vartype="hthr", varknots=40.3,
+         lagtype="integer", maxlag=5)
> basis.temp <- crossbasis(chicagoNMMAPS$temp, vartype="dthr", varknots=c(10,25),
+         lagtype="strata", lagknots=c(2,7), maxlag=15)
```

Here we make the assumption that the effect of O_3 is null up to 40.3 $\mu gr/m^3$ and then linear, applying an high threshold parameterization. For temperature, we use a double threshold with the

Figure 2

(a) (b)



assumption that the effect is linear below 10°C and above 25°C, and null in between. Regarding the lag dimension, we specify an unconstrained function for O_3, applying one parameter for each lag (`lagtype="integer"`) up to a 5 days. For temperature, we define 3 strata intervals at lag 0-1, 2-6, 7-15. A summary of the choices made for the cross-bases can be shown by the function `summary.crossbasis()`.

The estimates and predictions are carried out in the same way as in Section 5.2. The prediction range approximately equals the range of the observed values. The code is:

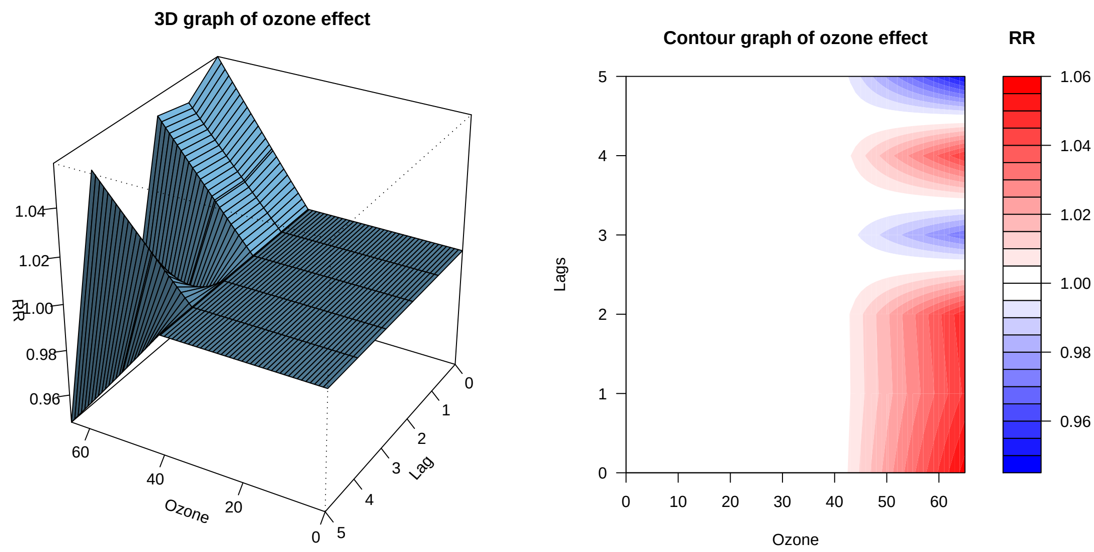
```
> model <- glm(death ~  basis.o3 + basis.temp, family=quasipoisson(), chicagoNMMAPS)
> pred.o3 <- crosspred(basis.o3, model,at=c(0:65,40.3,50.3))
```

The values for which the prediction must be computed are specified in `at`: here we define the integers from 0 to 65 μgr/m^3 (approximately the range), plus the threshold and the value 50.3 μgr/m^3 corresponding to a 10-unit increase above the threshold, which is set as the reference point (see *?crossbasis*). The vector is automatically ordered. Similarly to Section 5.2, we can also estimate and plot the overall effect of a 10-unit increase in O_3 with 95% confidence intervals. The commands are (results in Figures 2a-2b):

```
> crossplot(pred.o3, "slices", var=50.3, ci="bars",
+         title="Effect of a 10-unit increase in ozone along lags")
> crossplot(pred.o3,"overall",label="Ozone",
+         title="Overall effect of ozone over 5 days of lag")
```

Figure 3

(a) (b)



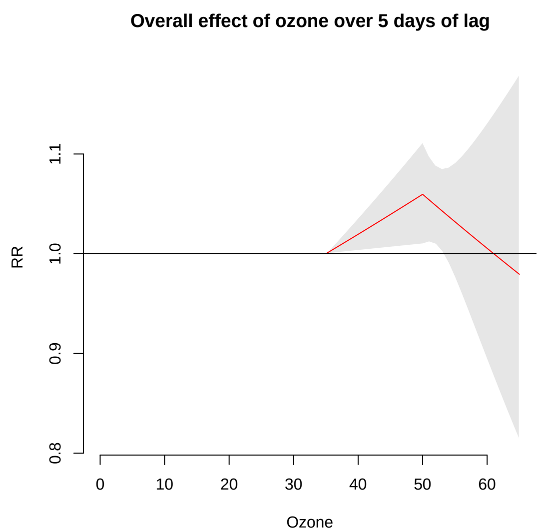
The confidence intervals for Figure 2a are represented by bars, as required by the argument `ci="bars"`.

In addition, we plot the three-dimensional effects (simultaneously along the spaces of O_3 and lags) using two other options of the function `crossplot()`. The argument `type="3d"` specifies a 3-D plot, while `type="contour"` builds a contour/level plot (Figures 3a and 3b):

```
> pred.o3$allRRfit["50.3"]

    50.3
1.045492

> cbind(pred.o3$allRRlow, pred.o3$allRRhigh)["50.3",]

[1] 1.010545 1.081647

> crossplot(pred.o3, label="Ozone", title="3D graph of ozone effect")
> crossplot(pred.o3, "contour", label="Ozone", title="Contour graph of ozone effect")
```

In order to illustrate a possible extension of the threshold models presented so far, we can assume that the O_3 effect is null up to 35 μgr/m^3 and then shows an additional change at 50 μgr/m^3. We can parameterize this effect with a piecewise linear function above a first threshold, changing slope at a specific cut-off point. Simply, we changed the cross-basis for O_3 including 2 `knots` which

Figure 4



specify the threshold and the cut-off point for the change in slope, then we updated the model and predicted the results under the new assumptions. The results, showed in Figure 4, can be compared with the same plot obtained under the simple threshold model in Figure 2b. :

```
> basis.o3 <- crossbasis(chicagoNMMAPS$o3, vartype="hthr", varknots=c(35,50),
+         lagtype="integer", maxlag=5)
> model <- update(model)
> pred.o3 <- crosspred(basis.o3, model, at=c(0:65))
> crossplot(pred.o3,"overall",label="Ozone",
+         title="Overall effect of ozone over 5 days of lag")
```

5.4 Example 3: a complex DLNM

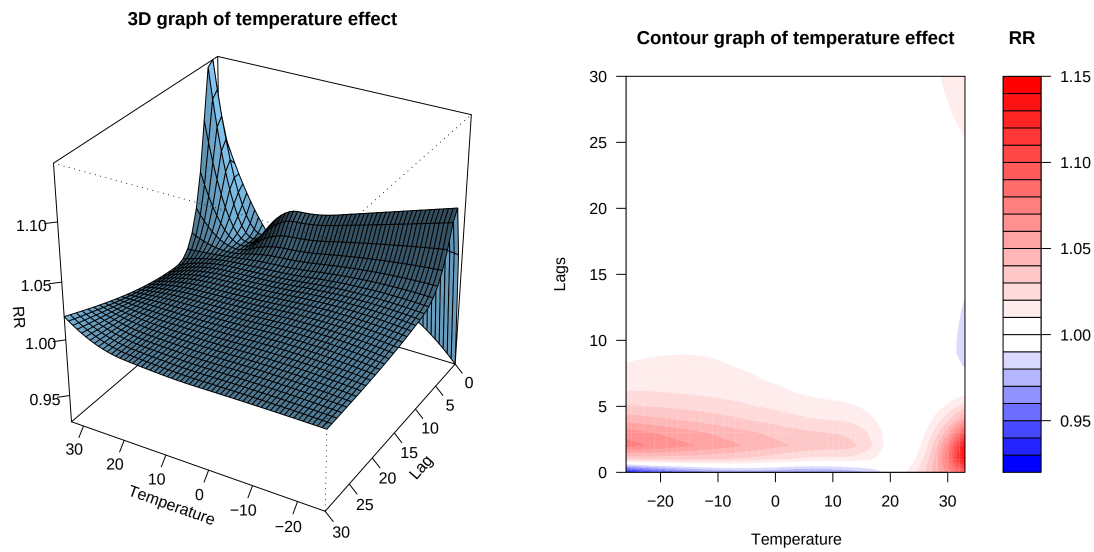
In this last example we specify a more complex DLNM, where the effects in both dimensions are estimated using smooth non-linear functions. Despite the higher complexity of the relationship, we will see how the steps required to specify and fit the model and predict and plot the results are exactly the same as for the simpler models see before in Sections 5.2-5.3. We apply this model to investigate the effects of temperature and PM_{10} on overall mortality up to lag 30 and 1, respectively.

These are the cross-basis matrices:

```
> basis.pm <- crossbasis(chicagoNMMAPS$pm10,vartype="lin", lagtype="strata",
+   cen=FALSE, maxlag=1)
> basis.temp <- crossbasis(chicagoNMMAPS$temp, vartype="bs", vardf=5, vardegree=2,
+   lagdf=5, cenvalue=21, maxlag=30)
```

Figure 5

(a) (b)



The chosen basis functions for the space of the predictor are a linear function for the effect of PM_{10} and a quadratic B-spline (`vartype="bs"`) with 5 degrees of freedom for temperature (with `varknots` placed by default at equally spaced quantiles in the space of the predictor). The basis for temperature is centered at 21°C, which will represent the reference point for the predicted effects. Regarding the space of lags, we assume a simple lag 0-1 parameterization for PM_{10} (i.e. a single strata up to lag 1, keeping the default values of `lagdf=1`), while we define another cubic spline, this time with the natural constraint (`vartype="ns"` by default) for the lag dimension of temperature. For this space, `lagknots` are located by default at equally spaced values in the log scale of lags, while the boundary knots are set to 0 and `maxlag`.

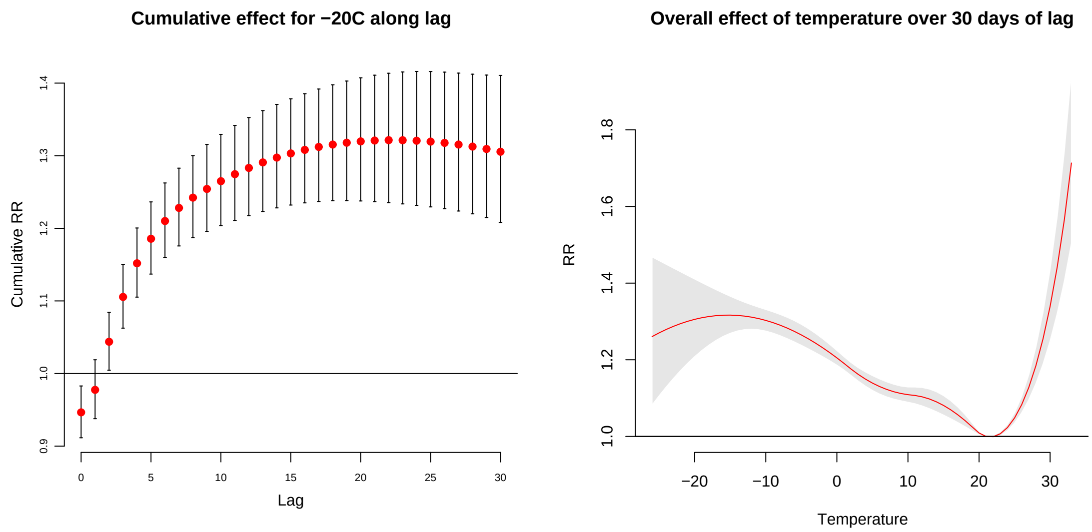
```
> model <- glm(death ~  basis.pm + basis.temp, family=quasipoisson(), chicagoNMMAPS)
> pred.temp <- crosspred(basis.temp, model, at=-26:33, cumul=TRUE)
> crossplot(pred.temp, label="Temperature",
+   title="3D graph of temperature effect")
> crossplot(pred.temp, "contour", label="Temperature",
+   title="Contour graph of temperature effect")
```

Note that cumulative effects have been predicted and included in the object `pred.temp` as a consequence of the argument `cumul=TRUE`. The 3-D and contour plots obtained by the commands above are represented in Figures 5a-5b.

The cumulative effects along lags for -20°C together with the overall effect are showed in Figures 6a-6b, and are obtained by:

Figure 6

(a) (b)




```
> crossplot(pred.temp, "slices", cum=TRUE, ci="bars", var=-20,
+   label="Temperature", title="Cumulative effect for -20C along lags")
> crossplot(pred.temp, "overall", label="Temperature",
+         title="Overall effect of temperature over 30 days of lag")
```

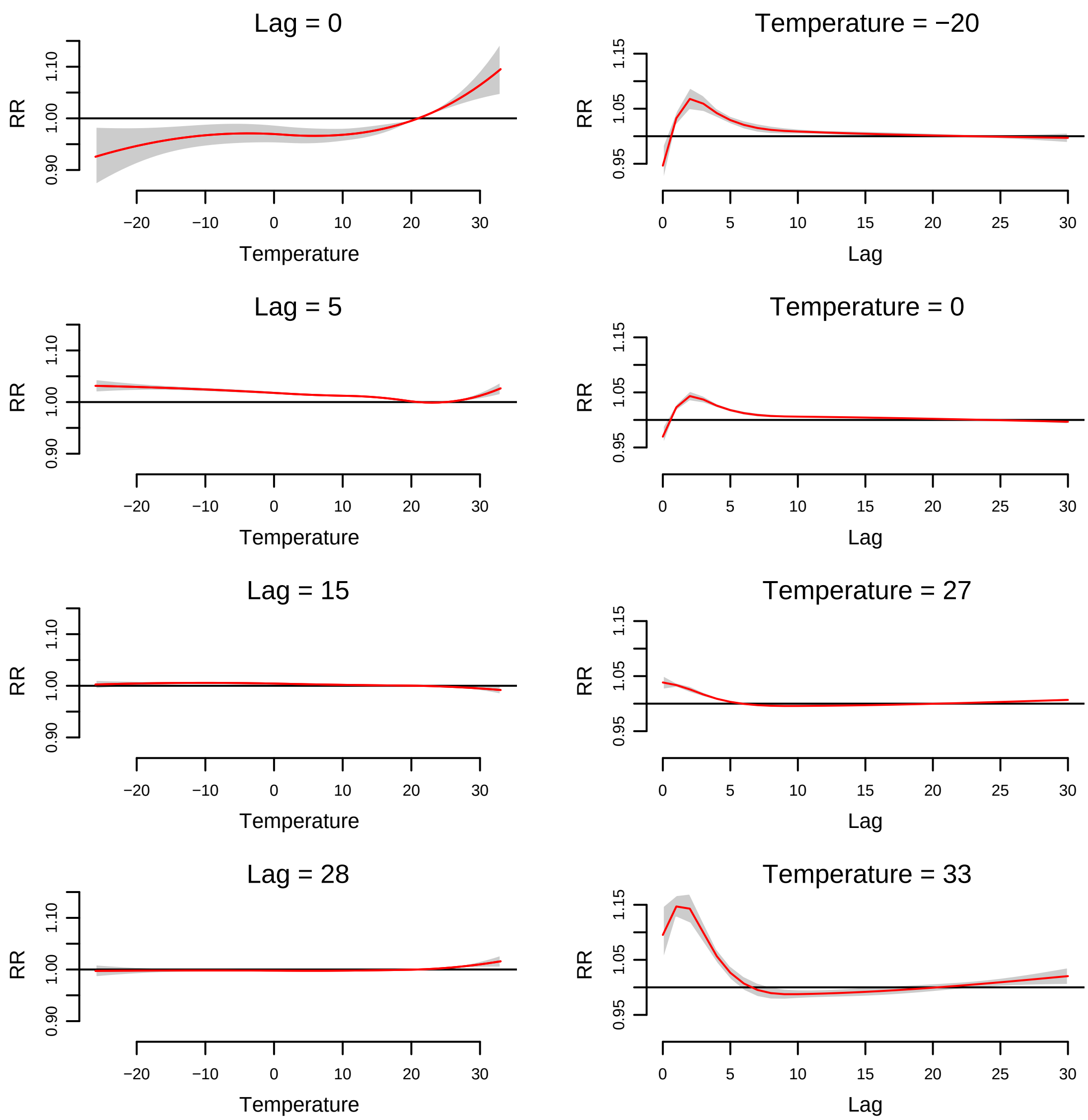
More comprehensively, Figure 7 shows the effects by temperature at multiple specific lags (left) and the effect by lag at multiple specific temperatures (right). The values in `var` and `lag` are used to define the specific predictor and lag values for which the effects must be computed. These plots can be imagined as the results of cutting "slices" on the effect surface shown in Figure 5a at the specific values of temperature and lags, and provide a detailed overview of the effects surface together with the related confidence intervals. This plot is carried out by:

```
> crossplot(pred.temp, "slices", var=c(-20,0,27,33),
+   lag=c(0,5,15,28), label="Temperature")
```

6 Conclusions

This document illustrates the functionalities of the dlnm package, providing a detailed overview of the process to specify and run a DLNM and then to predict and plot its results. The main advantage of this family of models is to unify many of the previous methods to deal with delayed effects in a unique framework, also providing more flexible alternatives regarding the shape of the relationships. Section 3 provides a brief summary of the theory underpinning DLNM's: a more

Figure 7


Lag = 0
RR
1.10
1.00
0.90
−20
−10
0
10
20
30
Temperature
Temperature = −20
RR
1.15
1.05
0.95
0
5
10
15
20
25
30
Lag
Lag = 5
Temperature = 0
Lag = 15
Temperature = 27
Lag = 28
Temperature = 33

detailed overview has been published elsewhere [3, 8], together with a complete specification of the algebra [8].

The flexibility is kept when this framework is implemented in the dlnm package: several different models with an increasing level of complexity can be performed using a simple and general procedure, as showed in the examples in Section 5. As already stated before, this method is not limited to the examples on the effect of air pollution and temperature on mortality, but can be applied to investigate the relationship between any predictor and outcomes in time-series data.

7 Acknowledgements

This work was supported by the Medical Research Council (UK) through the Research Grant RES-G0707030.

We gratefully acknowledge the valuable suggestions of Fabio Frascati regarding the procedures to build and document this package, and the authors of other package vignettes used as examples (especially Heather Turner and David Firth for the package gnm). Moreover, we are thankful to the colleagues who tested the beta-version of this package and suggested some important improvements included in the current version (in particular Marie-France Valois). The data included in the dataset `chicagoNMMAPS` are publicly available from the Internet-based Health and Air Pollution Surveillance System (iHAPSS) website (`http://www.ihapss.jhsph.edu`).

Finally, we express our gratitude to all the people working to develop and maintain the R Project.

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