trajeR package

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1 Introduction

Longitudinal data are the starting point for empirical research on numerous subjects in finance, economics, sociology, psychology, criminology and medicine and a host of statistical techniques are available for analyzing them (see Singer and Willet 2003, Gibobns et al. 2010 or Locascio and Atri 2011 for the general case or Verbeke and al. 2014 for multivariate data). The common statistical aim of these various application fields is the modelization of the evolution of an age or time-based phenomenon (Nagin 2002). Hence, the study of developmental trajectories is a central theme (Jones, Nagin & Roeder 2001; Sampson & Laub 1993). The objective of these approaches is to capture information about interindividual differences in intraindividual change over time (Nesselroade 1991). In the 1990s, the generalized mixed model assuming a normal distribution of unobserved heterogeneity (Bryk and Raudenbush 1992), multilevel modeling (Goldstein 1995), latent growth curves modeling (Muthén 1989, Willett and Sayer 1994) and the nonparametric mixture model, based on a discrete distribution of heterogeneity (Jones, Nagin and Roeder 2001) have emerged.

Growth mixture modeling, introduced by Muthén and Shedden (1999), is a very suitable framework to handle the issue of unobserved heterogeneity. Latent class growth analysis, also called nonparametric mixed model or semiparametric mixture model is the simplest specification of a growth mixture model. It allows no variation across individuals within classes. It was originally discussed by Nagin and Land (1993), Nagin (1999) and Roeder, Lynch and Nagin (1999) and is actually specifically designed to detect the presence of distinct subgroups among a set of trajectories and represents an interesting compromise between analysis around a single mean trajectory and case studies (Von Eye and Bergman 2003). Compared to subjective classification methods, the nonparametric mixed model has the advantage of providing a formal framework for testing the existence of distinct groups of trajectories. Andruff et al. (2009) conclude that latent class growth analysis serves as a steppingstone to growth mixture modeling analyses in which the precise number and shape of each trajectory must be known a priori in order for the researcher to impute the requisite start values for the model to converge in software packages such as Mplus (Jung and Wickrama, 2008).

While the conceptual aim of the analysis is to identify clusters of individuals with similar trajectories, the model's estimated parameters are not the result of a cluster analysis but of maximum likelihood estimation (Nagin 2005). Moreover, this method allows to evaluate the accuracy of the assignement of the individuals to the different sub-groups and to consider the variation of this accuracy in subsequent analyses (Dupéré et al. 2007). Nagin and Odgers (2010) document numerous applications of group-based trajectory modeling in criminology and clinical research. They state that the appeal of group-based trajectory modeling for the future lies in the potential for the innovative application of trajectory models on their own, in conjunction with other statistical methods or embedded within creative study designs while carefully considering the perils and pitfalls inherent in the use of any methodology.

Schiltz (Schiltz 2015) presents a generalization of Nagin's finite mixture model that allows non parallel trajectories for different values of covariates and different standard deviations for the disturbances in the different groups. This paper presents an R-package that analyzes longitudinal data by fitting the general finite mixture model.

The remainder of this article is structured as follows. In section two,we present

2 The generalized finite mixture model

As indicated above, we consider a population of size N divided into K latent classes, the assignment of an individual into which is based on the degree of similarity of the developmental trajectories of the individuals. This models supposes no structural between-subject variability within a class, hence the error variance is assumed to be constant inside a given class.

More precisely, consider a time-varying variable of interest Y defined in a population Ω of size N. Let $Y_i = y_{i_1}, \cdots, y_{i_T}$ be T measures of the variable Y, taken at times $t_1, \cdots, t_T$ for subject number i belonging to a sample of size n.
Furthermore, we suppose conditional independence for the sequential realizations of the elements y_{i_t} over the T periods of measurements, i.e. that a value y_{i_t} doesn't dependent on the past values $y_{i_{t'}}$, $t' < t$.

The aim of the analysis is to divide the population into K sub-populations, which are homogeneous in the sense that two subjects in the same group have similar trajectories for the variable of interest Y and two subjects in different groups have quite different trajectories for the variable of interest Y.

Let $P^k(Y_i)$ be the probability of Y_i given membership in group k (we note $G_i = k$, the latent group of individual i) and $P(Y_i)$ the unconditional probability of observing the realization Y_i of Y. Then,

$$P(Y_i) = \sum_{k=1}^{K} P\left(G_i = k\right) P^k(Y_i). \tag{1}$$

By definition of a finite mixture model (Nagin, 2005), the density f of Y is given by

$$f(y_i; \psi) = \sum_{k=1}^{K} \pi_k g_k(y_i; \Theta_k). \tag{2}$$

Here the group size $\pi_k > 0$ denotes the probability of a given subject to belong to group number k and thus

$$\sum_{k=1}^{K} \pi_k = 1.$$

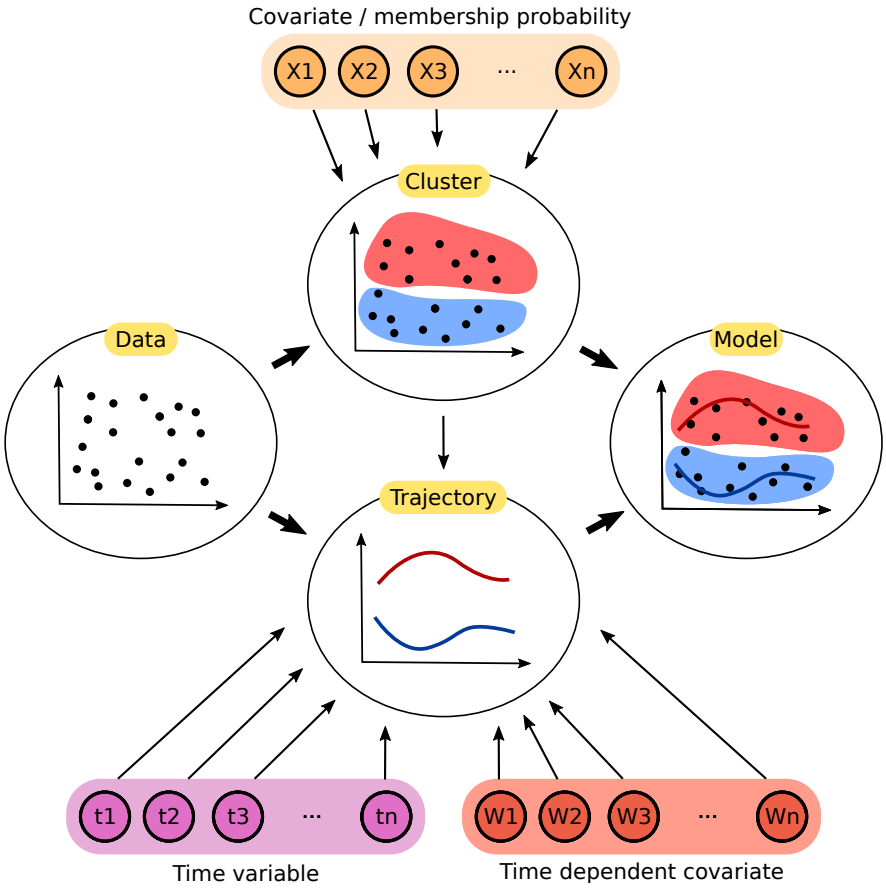
The role of the parameters Θ_k is to describe the shape of the trajectories in group k and hence the model depends on the parameter set $\psi = (K, \pi_1, \cdots, \pi_{K-1}, \Theta_1, \cdots, \Theta_K)$.

If we suppose moreover that the trajectories of Y are influenced by a static set of risk variables $X = (X_1 \cdots X_R)$, as well as by a time-dependent covariate W which is independent of X, we can write the conditional density of Y given X and W.

$$f\left(y_i | x_i, w_i\right) = \sum_{k=1}^{K} \left(P\left(G_i = k | X_i = x_i\right) \prod_{t=1}^{T} P\left(Y_{i_t} = y_{i_t} | X_i = x_i, W_i = w_i, G_i = k\right) \right), \tag{3}$$

which can be written as

$$f\left(y_i | x_i, w_i\right) = \sum_{k=1}^{K} \left(\sum_{j=1}^{R} \frac{e^{x_i^j \theta_k^j}}{1 + e^{x_i^j \theta_k^j}} \prod_{t=1}^{T} P\left(Y_{i_t} = y_{i_t} | W_i = w_i, G_i = k\right) \right). \tag{4}$$



Graphical representation of the model

The R-package trajeR allows to calibrate this model for different types of densities for Y. The package can indeed currently handle the following families of densities:

- Logit
- Censored Normal
- Zero Inflated Poisson.

We generally suppose that the trajectories follow a polynomial shape, but in case of an underlying normaldistribution, we include also the possibility of specifying any particular function for the shape of the trajectories, thus allowing for exponential functions for example.

This package extends the `traj` software for SAS or Stata written by Nagin and Jones (**jones_sas_2001**).

A complete description of the model and the proofs of all used algorithms inside this package can be found in Noel's PhD thesis (cf. `https://orbilu.uni.lu/`.) Basically, trajeR maximizes the log-likelihood by two methods : direct optimization of the derivative of the log-likelihood or the Expected Maximization Algorithm. For the direct optimization we use either the optim or the ucminf command. The Expected Maximization Algorithm is best suited to cases where we need to compute the Hessian matrix, whereas direct optimization of the derivative of the

log-likelihood works very well if there is no Hessian matrix to compute. In both cases, we use the quasi-Newton method BFGS, which calculates an iterative approximation of the inverse of the Hessian matrix. This is useful if the derivative of the function has sharp points or if the Hessian matrix is difficult to compute or becomes numerically singular. The Optim algorithm is used when we do not need to store the Hessian matrix otherwise TrajeR uses ucminf instead.

This package is written in R and C++. The linkage between R and C++ is achieved through the commands Rcpp (Eddelbuettel2013b) and RcppArmadillo.

3 Package design

The package `trajeR` is built around the core function `trajeR` which fits the model and computes its parameters for a given degree of polynomial shape. The function signature for `trajeR` is

```
R> trajeR(Y, A, Risk = NULL, TCOV = NULL, degre, degre.nu = 0,
+        Model, Method = "L",
+        ssigma = FALSE, ymax = max(Y) + 1, ymin = min(Y) - 1,
+        hessian = TRUE, itermax = 100, paraminit = NULL,
+        ProbIRLS = TRUE, refgr = 1,
+        fct = NULL, diffct = NULL, nbvar = NULL, nls.lmiter = 50)
```

Some of these arguments are mandatory others optional.

The mandatory arguments are the main data matrices Y, A, as well as degre, Model and Method.

Here Y is the matrix containing the values of the variable of interest and A is the matrix containing the age or time variable. In most applications, this matrix just contains times of measurement that are the same for each individual in the sample, implying that all lines of the matrix A are equal, but this is not necessarily the case. A can for instance contain the age of the different individuals at the times of measurement, which is generally different for each individual in the sample.
degre is a vector indicating the degree of the polynomials describing the typical trajectories in the different groups. Implicitely, the dimension of this vector also determines the number of groups into which we want to divide the population,
Model is a string defining the underlying distribution used in the model. The possibles choices are LOGIT for the Logistic Regression Mixture Model, CNORM for the Censored Normal Mixture Model or ZIP for the Zero Inflated Poisson Mixture model.
Method, finally, is a string to decide which algorithm is used for estimating the model parameters. The possible choices are `L` for direct optimization, `EM` for the Expectation Maximization algorithm with quasi-Newton procedures (for LOGIT and ZIP models) and `EMIRLS` for the Expectation Maximization algorithm using Iterative Weighted Least Squares.

The optional arguments are Risk, TCOV, degre.nu, ssigma, ymax, ymin, hessian, itermax, paraminit, ProbIRLS, refgr, fct, diffct, nls.lmiter, ng.nl and nbvar.

Risk is a data matrix that contains the values of the covariate X modifying the group membership probability. By default, there is no such variable and Risk is a one-column matrix with value 1. In case of the existence of a covariate X, it is treated by a classical multinomial logistic regression.
ProbIRLS allows to decide which method is used to compute the predictor probabilities. If

its value is TRUE (default setting) we use the IRLS method and if it is FALSE we use the optimization method.
TCOV is an optional data matrix containing a time-dependent covariate W that influences the trajectories themselves. By default its value is NULL.
To ensure the identifiability of the predictor, probability parameters, we have to fix a reference group. This can be done by the refgr command. It's default value is 1.
hessian indicates if we want to calculate the Hessian matrix, the default value being FALSE. If the method used is direct optimization, the Hessian matrix is computed by inverting the Fisher Information Matrix. To avoid numerically singular matrices we use FINIR. If the method is EM or EMIRLS, the Hessian matrix is computed by using the Louis method (Louis 1982).
itermax gives the maximal number of iterations for the optim function or for the EM algorithm.
The choice of the initial parameters is very important in optimization problems. We can specify these initial parameters by paraminit. By default trajeR calculates the initial value based on the range or the standard deviation of the data (Noel 2023).

In case of a Zero Inflated Poisson model, we have to specify the probability to belong to the excess zero state. This is done by using a polynomial logistic regression. degre.nu is the degree of the polynomial.

In case of a Censored Normal model, we have to define several arguments. ssigma indicates if we suppose to have the same standard deviation for the error terms in all groups. By default, its value is FALSE. ymax indicates the maximum of Y. It concerns only the model with censored data. By default its value is the maximum value of the data plus 1, i.e the model used is simply the normal model. Likewise, ymin indicates the minimum of Y.

There are also several arguments to define in order to use general nonlinear functions for the typical trajectories in the different groups. fct gives the definition of the function used to define the shape of the trajectories and its differential is defined in diffct. Here too, we have to specify the number of groups to use by nl.ng,nbvar, nls.lmiter

The output of trajeR is an object of class Trajectory that can be of four types depending on the model used: Trajectory.LOGIT, Trajectory.CNORM, Trajectory.ZIP or Trajectory.NL. These classes are described in the following sections.

4 The LOGIT model

For the finite mixture model with underlying binary logit distribution, called here the LOGIT model, we consider a latent variable y_{it}^* such that

$$y_{it}^* = f(a_{it}; \beta_k, \delta_k) + \varepsilon_{it} = \beta_k A_{it} + \delta_k W_t + \varepsilon_{it}, \tag{5}$$

where $\varepsilon_{it} \sim \mathcal{N}(0,\ \sigma_k)$, $A_{it} = (1, a_{it}, a_{it}^2, \cdots, a_{it}^{n_\beta - 1})^t$, $W_t = (w_{i1}, \cdots, w_{in_\delta})^t$, $\beta_k = (\beta_{k1}, \cdots, \beta_{kn_\beta})$ and $\delta_k = (\delta_{k1}, \cdots, \delta_{kn_\delta})$, n_δ denotes the dimension of the covariate W and n_β the number of measurements of Y for every individual.
The usual assumption is that the binary variable $y_{it} = 1$ if $y_{it}^* > 0$ and $y_{it} = 0$ if $y_{it}^* \leq 0$.

The probit function $\rho_{ikt} = P(Y_{it} = 1 | W_i = w_i, G_i = k)$ denotes the probability of $y_{it} = 1$

given membership in group k. We have

$$\rho_{ikt} = \frac{e^{\beta_k A_{it} + \delta_k W_{it}}}{1 + e^{\beta_k A_{it} + \delta_k W_{it}}}. \tag{6}$$

Thus,

$$g_k(y_i; \beta_k, \delta_k) = \prod_{t=1}^{T} \left(\frac{e^{\beta_k A_{it} + \delta_k W_{it}}}{1 + e^{\beta_k A_{it} + \delta_k W_{it}}} \right)^{y_{it}} \left(\frac{1}{1 + e^{\beta_k A_{it} + \delta_k W_{it}}} \right)^{1 - y_{it}} \tag{7}$$

and the log likelihood of the model is given by

$$l(\psi; y) = \sum_{i=1}^{n} \log \left(\sum_{k=1}^{K} \pi_k \prod_{t=1}^{T} \left(\frac{e^{\beta_k A_{it} + \delta_k W_{it}}}{1 + e^{\beta_k A_{it} + \delta_k W_{it}}} \right)^{y_{it}} \left(\frac{1}{1 + e^{\beta_k A_{it} + \delta_k W_{it}}} \right)^{1 - y_{it}} \right). \tag{8}$$

The output of the trajeR function gives an object of class trajectory.LOGIT, which is a list containing at least the following components:

Component	Description
beta	a vector with the beta parameters
delta	a vector with the delta parameters (only exists in case of a covariate function W).
theta	a vector with the theta parameters (only exists in case of a covariate function X).
sd	a vector with the standard deviations of the estimated parameters.
tab	a matrix with all estimated parameters and their standard deviations.
model	a string stating which model was used.
groups	an integer giving the number of groups.
Names	the names of the beta parameters (intercept, linear, quadratic...)
Method	a string stating which method was used.
Size	an integer giving the sample size.
Likelihood	a real number giving the likelihood of the model.
Time	a vector with the time points ie the first line of matrix A
degre	a vector with the degrees of the typical polynomial trajectories in the different groups.

4.1 Simulation example

We use the simulated dataset LOGIT_data01 that comes with installing the package from the CRAN repository. The sample consists of 500 trajectories with 10 time-points each, the values of the variable Y being 0 or 1. The dataset consists in a simulated 3 group solution, the parameters of which are summarized in the following table

Parameters	β_{k0}	β_{k1}	β_{k2}	β_{k3}	β_{k4}	π_k
Group 1	-2.26	-0.109	0.14	-0.011		0.22
Group 2	1.291	0.811	-0.554	0.077	-0.003	0.44
Group 3	-1.99243					0.34

The variable of interest Y_i is contained in `data[,2:11]`, the time variable A_i in `data[,12:21]`, the time-dependent covariate W, which could for instance indicate the presence of a characteristics of the individual, in `data[,24:33]` and a covariate X influencing group membership

probabilty in `data[,48:49]`. Hence,

`data[,2:11]`	is a matrix with values 0 and 1.
`data[,12:21]`	is a matrix with time points from 1 to 10.
`data[,22:23]`	is a matrix with values 0 and 1.
`data[,24:33]`	is a matrix with values 0 and 1.

Usually, we first plot the data to have a first impression about it,but this does not make a lot of sense here, since our variable of interest is dichotomous.

First, we use trejR to calibrate the basic finite mixture model. We run it once for each method. In both applications, we specify the number of group to be 3 by putting 3 values into the parameter degre. In a real-life situation, we would of course needed to find the optimal number of groups, as well as the optimal degree for the polynomial trajectories for each group by an exploratory procedure. Here, we know that we simulated data with polynomials of degree 0, 3 and 4 respectively for the three groups. Hence, degree is the vector $(0, 3, 4)$.
Moreover, we specify hessian=TRUE to ask the computation of the Hessian matrix and set Itermax to 300 to ensure a good approximation of the parameters.

For the Likelihood method we call the trajeR function with parameter Method ="L".

```
R> # Likelihood
R> solL = trajeR(Y = data[,2:11], A = data[,12:21],
+                degre = c(0,3,4),
+                Model = "LOGIT", Method = "L", hessian = TRUE)

The output of \code{trajeR} gives the following parameter
estimations:

Model : Logit
Method : Likelihood

  group   Parameter   Estimate   Std. Error   T for H0:   Prob>|T|
                                              param.=0
-----------------------------------------------------------------
      1   Intercept   -1.94514      0.11033   -17.63067          0

      2   Intercept   -1.78181       1.2588    -1.41549    0.15699
             Linear     -0.426      0.64991    -0.65547    0.51219
          Quadratic     0.1834      0.10798     1.69848    0.08948
              Cubic   -0.01211      0.00574    -2.11149    0.03478

      3   Intercept    1.74118      0.75191     2.31567    0.02062
             Linear     0.6527      0.76836     0.84947    0.39566
          Quadratic   -0.55852       0.2571    -2.17237    0.02987
              Cubic    0.08247      0.03354     2.45865    0.01398
            Quartic   -0.00338      0.00149    -2.26099     0.0238
-----------------------------------------------------------------
      1         pi1    0.41814      0.03917           0          0
      2         pi2    0.21874       0.0455    -14.2397          0
      3         pi3    0.36312      0.03533    -3.99337          0
```

```
-----------------------------------------------------------------------
Likelihood : -2852.746
```

For the EM method, we call the trajeR function with parameter Method = "EM" or Method = "EMIRLS".

```
R> #EM
R> solEM = trajeR(Y = data[,2:11], A = data[,12:21],
+                 degre = c(0,3,4),
+                 Model = "LOGIT", Method = "EM", hessian = TRUE,
+                 itermax = 500)
R> #EMIRLS
R> solEMIRLS = trajeR(Y = data[,2:11], A = data[,12:21],
+                      degre=c(0,3,4),
+                      Model = "LOGIT", Method = "EMIRLS", hessian = TRUE,
+                      itermax = 500)
```

The output of trajeR gives the following parameter estimations (we added the previous estimations for the likelihood method as first column for easier comparison):

SolL		SolEM		SolEMIRLS	
parameters	sd	parameters	sd	parameters	sd
Beta 1					
-1.94514	0.11033	-1.94767	0.09785	-1.94514	0.09673
Beta 2					
-1.78181	1.25880	-1.34108	0.81569	-1.78180	1.01371
-0.42600	0.64991	-0.61486	0.49090	-0.42600	0.58510
0.18340	0.10798	0.20768	0.09134	0.18340	0.10483
-0.01211	0.00574	-0.01308	0.00517	-0.01211	0.00578
Beta 3					
1.74118	0.75191	1.75148	0.80594	1.74118	0.76282
0.65270	0.76836	0.79019	0.81425	0.65271	0.77462
-0.55852	0.25710	-0.61230	0.26768	-0.55852	0.25545
0.08247	0.03354	0.08893	0.03451	0.08247	0.03302
-0.00338	0.00149	-0.00362	0.00152	-0.00338	0.00146
Pi					
0.41814	0.03917	0.41731	0.02973	0.41814	0.02941
0.21874	0.04550	0.23236	0.02973	0.21874	0.02941
0.36312	0.03533	0.35033	0.04085	0.36312	0.04051

We see that the parameter estimations for the different methods are very similar. As a verification, we also calibrated the model with the procTraj software and also found very similar results.

In a second step, we suppose that the membership probability depend on some covariate X. In our example, X is stored in `data[,22:23]` and has only the values 0 or 1.
We need to specify a reference group, the effect of the risk variavle is comapred to. By default, this reference group is the first group, but this can be changed by the parameter refgr. As before, we first calibrate the model by using the likelihood method.

```
R> solLRisk = trajeR(Y = data[,2:11], A = data[,12:21], Risk = data[,22:23],
+                    degre = c(0,3,4),
+                    Model = "LOGIT", Method = "L", hessian = TRUE,
+                    itermax = 300)
```

The results

```
R> solLRisk
```

```
The output of \code{trajeR} gives the following parameter
estimations:

 Model : Logit
 Method : Likelihood

  group   Parameter   Estimate   Std. Error   T for H0:   Prob>|T|
                                              param.=0
-----------------------------------------------------------------------
      1   Intercept   -1.93481      0.10685   -18.10702          0

      2   Intercept   -4.48563      4.53011    -0.99018    0.32213
             Linear    0.88044      2.24991     0.39132    0.69557
          Quadratic    -0.0103      0.34631    -0.02975    0.97627
              Cubic    -0.0031      0.01681    -0.18432    0.85377

      3   Intercept    1.65457      0.71638     2.30962    0.02095
             Linear    0.49525      0.69724      0.7103    0.47755
          Quadratic     -0.492      0.23246    -2.11649    0.03435
              Cubic    0.07471      0.03044     2.45432    0.01415
          Quadratic   -0.00311      0.00136    -2.28584    0.02231
-----------------------------------------------------------------------
      1    Baseline          0           NA          NA         NA

      2   Intercept   -0.99839      0.42801    -2.33262    0.01971
                 X1   -0.07154      0.33726    -0.21213    0.83201
                 X2    0.36804      0.34079     1.07994    0.28022

      3   Intercept    0.22836       0.2082     1.09683    0.27277
                 X1   -0.24236      0.22869    -1.05976     0.2893
                 X2   -0.38481      0.23851    -1.61338    0.10673
-----------------------------------------------------------------------
Likelihood : -2849.035
```

We then launch the function trajeR with parameters EM and EMIRLS too. In this case, the convergence is quite slow.

```
R> solEMRisk = trajeR(Y = data[,2:11], A = data[,12:21], Risk = data[,22:23],
+        degre = c(0,3,4),
+        Model = "LOGIT", Method = "EM", hessian = TRUE,
+        itermax = 500)
```

```
R> solEMIRLSRisk = trajeR(Y = data[,2:11], A = data[,12:21], Risk = data[,22:23],
+                     degre = c(0,3,4),
+                     Model = "LOGIT", Method = "EMIRLS", hessian = TRUE,
+                     itermax = 500)
```

The results of all methods are summarized in the following table:

SolLRisk		SolEMRisk		SolEMIRLSRisk	
par.	sd	par.	sd	par.	sd
Beta 1					
-1.93481	0.10685	-1.94620	0.17254	-1.93481	0.16177
Beta 2					
-4.48563	4.53011	-2.60317	2.20347	-4.48559	4.28713
0.88044	2.24991	-0.03748	1.11646	0.88043	2.13965
-0.01030	0.34631	0.12704	0.18039	-0.01030	0.33488
-0.00310	0.01681	-0.00956	0.00899	-0.00310	0.01631
Beta 3					
1.65457	0.71638	1.75301	0.75324	1.65458	0.74570
0.49525	0.69724	0.53393	0.73734	0.49525	0.68429
-0.49200	0.23246	-0.51353	0.24797	-0.49200	0.22824
0.07471	0.03044	0.07709	0.03209	0.07471	0.02982
-0.00311	0.00136	-0.00317	0.00141	-0.00311	0.00133
Theta - First group 0					
-0.99839	0.42801	-0.81927	0.61012	-0.99838	0.60966
-0.07154	0.33726	-0.10292	0.32779	-0.07154	0.33379
0.36804	0.34079	0.28454	0.36585	0.36804	0.37889
0.22836	0.20820	0.19350	0.27754	0.22836	0.26728
-0.24236	0.22869	-0.24076	0.23522	-0.24236	0.23082
-0.38481	0.23851	-0.38691	0.24532	-0.38481	0.23352

Finally, let's see an example, where we have some time-dependent covariate that influences the shape of the trajectories itself. We consider these effects by using the option TCOV in the command trajeR.
In our data, the time-dependant covariate is stored in data[,24:33] and has only the values 0 or 1. We again calibrate the model by using the three available methods.

In order to run the algorithm with sensible initial values, we use the results of the example without time covariate as parameter initialisation.

```
R> paraminitL = c(solL$theta[-1], solL$beta, #solution without time covariate
+                 0,0,0 # initial values for TCOV)
```

Then we launch the function trajeR

```
R> solLTCOV = trajeR(Y = data[,2:11], A =data[,12:21], TCOV = data[,24:33],
+                     degre = c(0,3,4),
+                     Model = "LOGIT", Method = "L", hessian = TRUE,
+                     itermax = 300, paraminit = paraminitL)
```

We get the following result.

```
Model : Logit
Method : Likelihood

  group   Parameter   Estimate   Std. Error   T for H0:   Prob>|T|
                                              param.=0
-----------------------------------------------------------------------
      1   Intercept   -2.01725      0.14515   -13.89748          0
              TCOV1    0.14188      0.17204     0.82469    0.40959

      2   Intercept   -1.84958      1.29591    -1.42724    0.15357
             Linear   -0.42661      0.68006    -0.62731    0.53048
          Quadratic    0.18422      0.11409     1.61473    0.10643
              Cubic   -0.01217      0.00608    -2.00396    0.04513
              TCOV1    0.11965      0.19659     0.60862    0.54281

      3   Intercept    1.72138      0.75409     2.28274    0.02249
             Linear    0.66141      0.77181     0.85696    0.39151
          Quadratic    -0.5608      0.25664    -2.18518    0.02892
              Cubic     0.0827      0.03316     2.49368    0.01267
          Quadratic   -0.00339      0.00146    -2.31694    0.02055
              TCOV1    0.01868      0.11427     0.16347    0.87016
-----------------------------------------------------------------------
      1         pi1     0.4187      0.03863           0          0
      2         pi2    0.21781      0.04533   -14.41866          0
      3         pi3     0.3635       0.0339     -4.1711          0
-----------------------------------------------------------------------
Likelihood : -2851.937
```

For the EM algorithm, in the initialization step, we have to transform the theta parameters to a probability.

```
R> paraminitEM = c(exp(solL$theta)/sum(exp(solL$theta)),
+                  solL$beta,  # solution without time covariate
+                  0,0,0 # initial values for TCOV)

R> solEMTCOV = trajeR(Y = data[,2:11], A = data[,12:21], TCOV = data[,24:33],
+                     degre = c(0,3,4),
+                     Model = "LOGIT", Method = "EM", hessian = TRUE,
+                     itermax = 300, paraminit = paraminitEM)
R> solEMIRLSTCOV = trajeR(Y = data[,2:11], A = data[,12:21], TCOV = data[,24:33],
+                         degre = c(0,3,4),
+                         Model = "LOGIT", Method = "EMIRLS", hessian = TRUE,
+                         itermax = 300, paraminit = paraminitEM)
```

We get the following results:

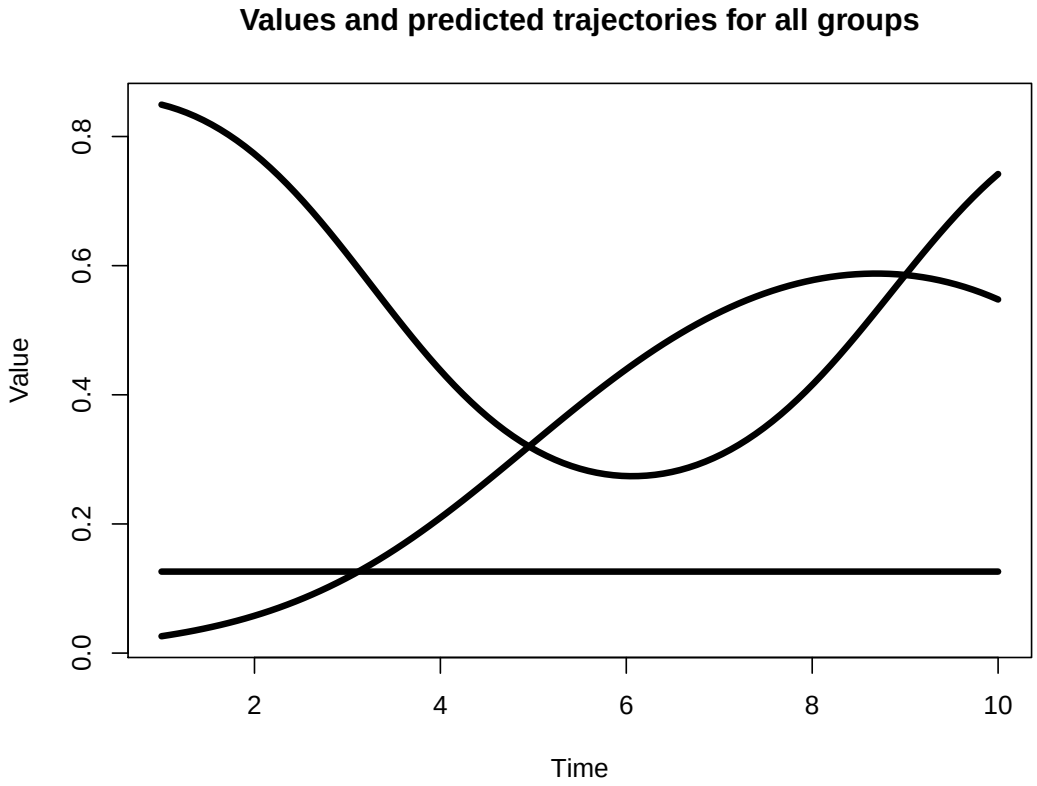
SolLTCOV		SolEMTCOV		SolEMIRLSTCOV	
par.	sd	par.	sd	par.	sd
Beta 1					
-2.01725	0.14515	-2.01680	0.13886	-2.01725	0.13877
Beta 2					
-1.84958	1.29591	-1.81020	0.99890	-1.84956	1.01962
-0.42661	0.68006	-0.44369	0.57625	-0.42662	0.58628
0.18422	0.11409	0.18646	0.10379	0.18422	0.10524
-0.01217	0.00608	-0.01226	0.00574	-0.01217	0.00581
Beta 3					
1.72138	0.75409	1.74532	0.76778	1.72138	0.76171
0.66141	0.77181	0.65570	0.77775	0.66141	0.77300
-0.56080	0.25664	-0.56069	0.25630	-0.56080	0.25495
0.08270	0.03316	0.08273	0.03312	0.08270	0.03296
-0.00339	0.00146	-0.00339	0.00146	-0.00339	0.00146
Delta 1					
0.14188	0.17204	0.14147	0.17279	0.14188	0.17277
Delta 2					
0.11965	0.19659	0.12019	0.19750	0.11965	0.19811
Delta 3					
0.01868	0.11427	0.01657	0.11479	0.01868	0.11446
Pi					
0.41870	0.03863	0.41878	0.02952	0.41870	0.02949
0.21781	0.04533	0.21898	0.02792	0.21781	0.02789
0.36350	0.03390	0.36224	0.04063	0.36350	0.04059

4.2 Plots

There are different possibilities to present the results graphically. The basic graph consists in plotting the typical trajectories of the different groups. This can be done with the standard plot function of R applied to an object of class Trajectory. For instance, to plot the solution of the model with risk covariate, we simplify write

```
R> plot(solLRisk)
```

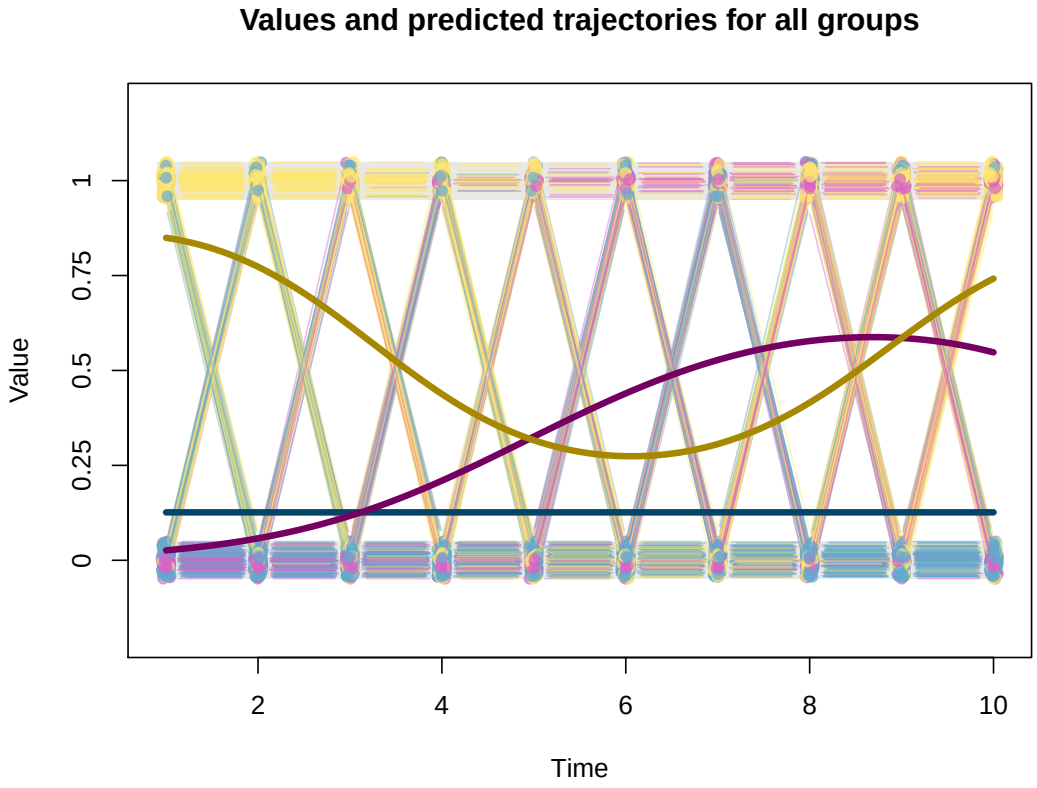
to get the following plot



We can also add the individual trajcetories to the graph, with different colors for the different groups. For this, we have to specify Y and A in the function plot().
For a better visibility, we use the parameter dec = 5, which helps to visualize the data by allowing for thicker lines in case of multiple individuals with the same trajectory.

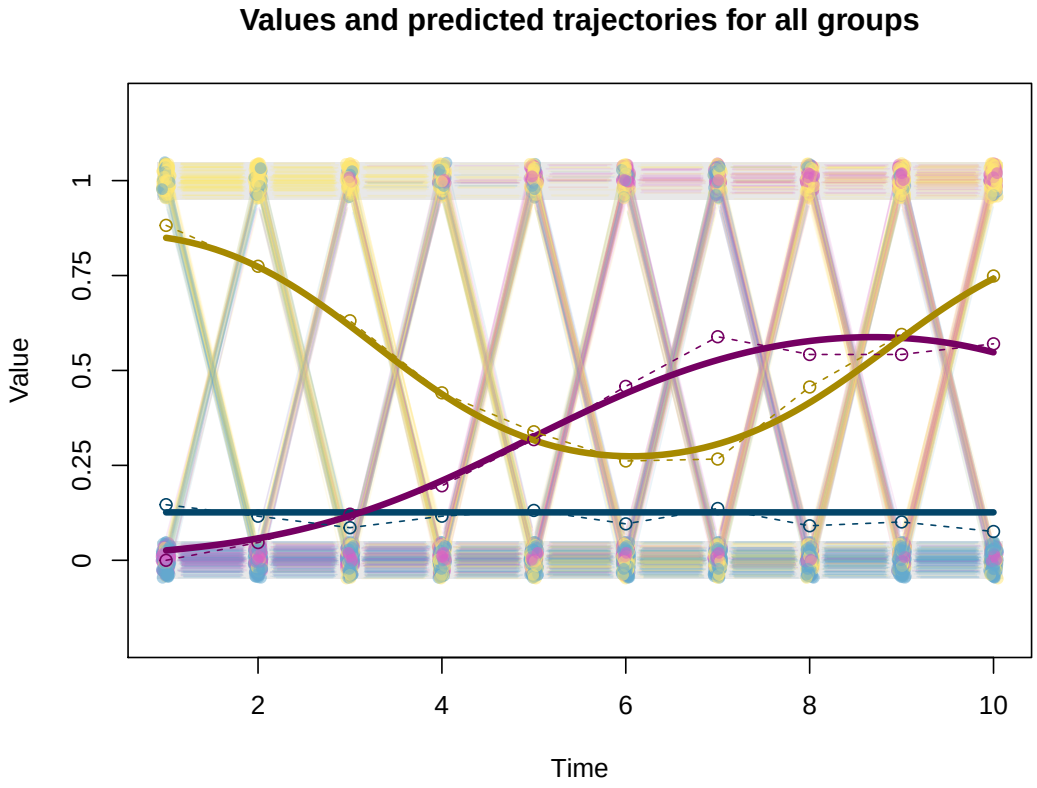
By default, the colors used for the graph are gray scale, but we can manually specify any colors we want. In that case, we need to specify to colors for each groups, one for the individual trajectories and one for the typical group trajectory.

```
R> # colour's defintion
R> trans = "70"
R> col1 = "#034569"
R> col1.1 = paste0("#64AAD0", trans)
R> col2 = "#750062"
R> col2.1 = paste0("#D962C7", trans)
R> col3 = "#A68900"
R> col3.1 = paste0("#FFE773", trans)
R> cols1 = c(col1.1, col2.1, col3.1)
R> cols2 = c(col1, col2, col3)
R> vcol = c(cols1, cols2)
R>
R> plot(solLRisk, Y = data[,2:11], A = data[,12:21], dec = 5, col = vcol)
```



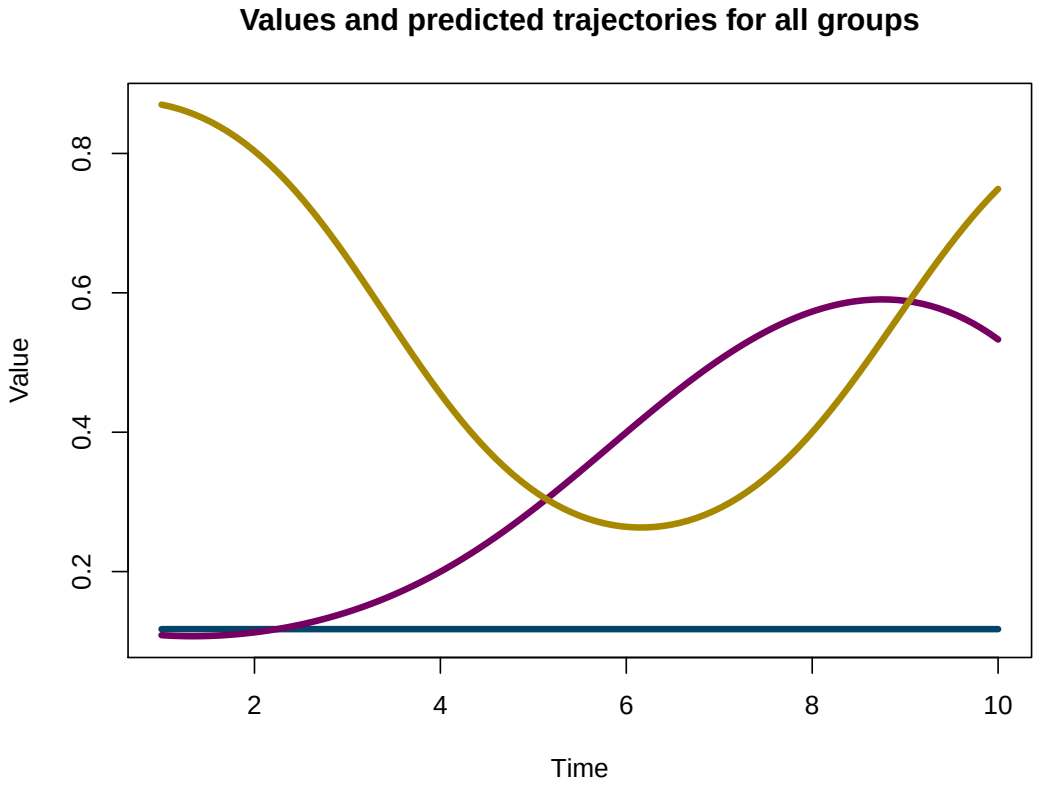
Notice that there is a difference between the typical trajectories estimated by the model for each group and the average group trajectories. The typical trajectories are indeed polynomials of degree smaller than four, whereas the average trajectories can follow any function. We can add the average of the data points on the graph by using mean = TRUE.

```
R> plot(solLRisk, Y = data[,2:11], A = data[,12:21], dec = 5, +
col = vcol, mean = TRUE, alpha = 0.3)
```



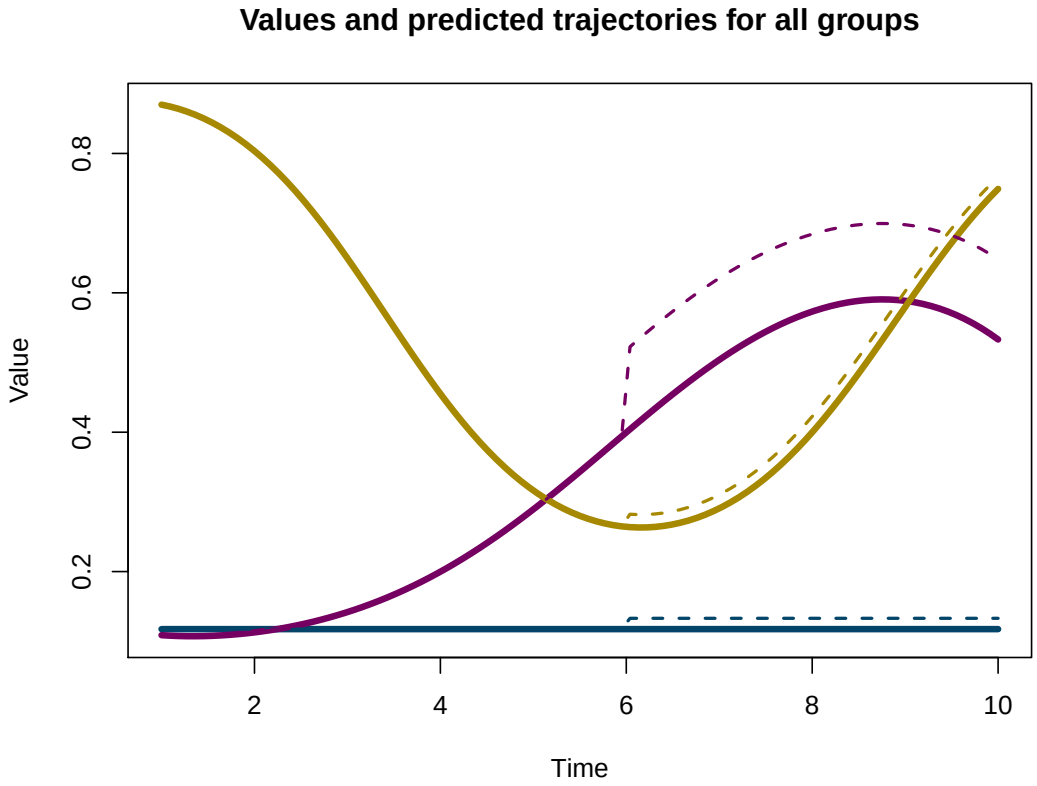
For the example with a time-dependent covariate influencing the trajectories, we get the following typical trajectories:

```
R> plot(solLTCOV, col = vcol)
```



If we want show the impact of a particular value of the time covariate on the trajectory, we can add this to the plot by using the `plotcov` parameter.
The full lines give the typical trajectories taking the time-dependent covariate into account, whereas and the dashed lines show the impact of a particular value of the covariate on the trajectories.

```
R> plot(solLTCOV, col = vcol, plotcov = c(0,0,0,0,0,1,1,1,1,1))
```



In our example, we see that the covariate has no influence before time 6. Afterwards, the covariate has only a small influence in the blue and yellow groups, but its impact in the purple group is quite big.

5 Censored Normal model

For the censored normal model, we consider a latent variable y_{it}^* such that

$$y_{it}^* = f(a_{it}; \beta_k, \delta_k) + \varepsilon_{k,it} = \beta_k A_{it} + \delta_k W_{it} + \varepsilon_{k,it} \tag{9}$$

where $\varepsilon_{k,it} \sim \mathcal{N}(0;\ \sigma_k)$, $A_{it} = (1, a_{it}, a_{it}^2, \cdots, a_{it}^{n_\beta - 1})^t$, $W_{it} = (w_{i1}, \cdots, w_{in_\delta})^t$, $\beta_k = (\beta_{k1}, \cdots, \beta_{kn_\beta})$ and $\delta_k = (\delta_{k1}, \cdots, \delta_{kn_\delta})$.
It is easy to suppose that the variable Y is a censored variable, since the values of the data are always between two bounds y_{min} and y_{max}.
So we can link y_{it}^* to the observed and censored data y_{it} by

$$y_{it} = y_{min} \text{ if } y_{it}^* < y_{min} \tag{10}$$
$$y_{it} = y_{it}^* \text{ if } y_{min} \leq y_{it}^* \leq y_{max} \tag{11}$$
$$y_{it} = y_{max} \text{ if } y_{it}^* > y_{max}. \tag{12}$$
$$\tag{13}$$

Denote $\mu_{ikt} = \beta_k A_{it} + \delta_k W_t$. Then

$$P(Y_{it} = y_{it}|W_i = w_i, G_i = k) = \begin{cases} \Phi\left(\dfrac{y_{min} - \mu_{ikt}}{\sigma_k}\right) & \text{if } y^*_{it} < y_{min} \\ \dfrac{1}{\sigma_k}\phi\left(\dfrac{y_{it} - \mu_{ikt}}{\sigma_k}\right) & \text{if } y_{min} \leq y^*_{it} \leq y_{max} \\ 1 - \Phi\left(\dfrac{y_{max} - \mu_{ikt}}{\sigma_k}\right) & \text{if } y^*_{it} > y_{max} \end{cases}, \tag{14}$$

where Φ and ϕ denote the cumulative distribution function and density of a standard centered normal law.

Thus, $g_k\left(y_i|;\beta_k, \delta_k, \sigma_k\right)$ becomes

$$\prod_{y_{it}=y_{min}} \Phi\left(\frac{y_{min} - \mu_{ikt}}{\sigma_k}\right) \prod_{y_{min}<y_{it}<y_{max}} \frac{1}{\sigma_k}\phi\left(\frac{y_{it} - \mu_{ikt}}{\sigma_k}\right) \prod_{y_{it}=y_{max}} \left(1 - \Phi\left(\frac{y_{max} - \mu_{ikt}}{\sigma_k}\right)\right) \tag{15}$$

and

$$l(\psi; y) = \sum_{i=1}^{n} \log\left(\sum_{k=1}^{K} \pi_k g_k(y_i; \beta_k, \delta_k, \sigma_k)\right).$$

The output of the trajeR function is an object of class trajectory.CNORM, i.e. a list containing at least the following components:

Parameters	Description
beta	a vector with the beta parameters.
sigma	a vector with the sigma parameters.
delta	a vector with the delta parameters (only exists if we use covariate function W).
theta	a vector with the theta parameters (only exists if we use covariate function X).
sd	a vector of the standard deviation of the parameters.
tab	a matrix with all parameters and their standard deviation.
model	a string stating which model was used.
groups	a integer giving the number of groups.
Names	the names of the beta parameters (intercept, linear, quadratic...).
Method	a string stating which method was used.
Size	an integer giving the sample size.
Likelihood	a real number giving the likelihood of the model.
Time	a vector with the time points ie the first line of matrix A.
degre	vector with the degrees of the typical polynomial trajectories in the different groups.
min	a real number giving the minimum of Y.
max	a real number giving the maximum of Y.

5.1 Simulation example

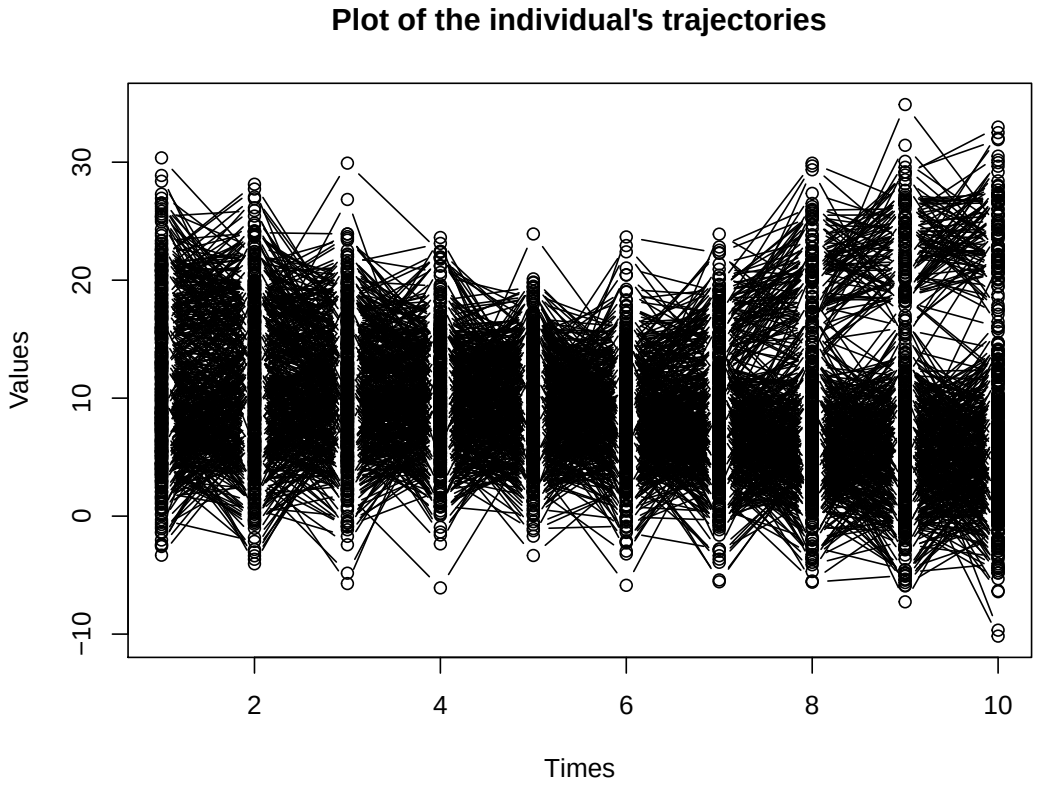
We use the simulated dataset CNORM_data01 contained in the library. The sample consists of 500 trajectories with 10 time-points each. We simulate a 3 group solution, the parameters of which are summarized in the following table

Parameters	β_{k0}	β_{k1}	β_{k2}	β_{k3}	β_{k4}	π_k	σ_k
Group 1	2.797	8.809	-3.201	0.463	-0.021	0.32	4
Group 2	7					0.54	4
Group 3	19.545	-0.297	-0.407	0.026		0.14	4

The variable of interest Y is contained in `data[,2:11]`, the time variable A in `data[,12:21]`, the time-dependent covariate W in `data[,22:41]` and a covariate X influencing group membership probability in `data[,42:43]`. Hence,

`data[,2:11]`	is a matrix with real numbers.
`data[,12:21]`	is a matrix with time points from 1 to 10.
`data[,22:31]`	is a matrix with values 0 and 1, indicating the presence or absence of a certain characteristics of the individual.
`data[,32:41]`	is a with real numbers.
`data[,42:43]`	is a matrix with values 0 and 1.

First we plot the data to get a first impression.



Again, we start by fitting the basic finite mixture model. We use each method to fit the model. In both applications, we specify the number of group to be 3 by putting 3 values into the parameter degre. We know that we simulated data with polynomials of degree 0, 3 and 4 respectively for the three groups. Hence, degree is the vector $(0, 3, 4)$.
Moreover, we specify hessian=TRUE to ask the computation of the Hessian matrix and set

Itermax to 300 to ensure a good approximation of the parameters.

For the Likelihood method we call `trajeR` with option `Method ="L"`. The parameters `ssigma` allows to specify if we want the same σ in each group. ssigma = FALSE specifies that we have different variability in the different groups.

```
R> # Likelihood different sigma
R> solL = trajeR(Y = data[,2:11], A = data[,12:21],
+                degre = c(0,3,4),
+                Model = "CNORM", Method = "L",
+                hessian = TRUE, ssigma = FALSE)
```

We get the following result:

```
Model : Censored Normal
Method : Likelihood

  group   Parameter   Estimate   Std. Error   T for H0:   Prob>|T|
                                              param.=0
-------------------------------------------------------------------
      1   Intercept     7.0494      0.08442    83.50741          0

      2   Intercept   19.30454       0.6537    29.53102          0
             Linear   -0.09315      0.48451    -0.19225    0.84755
          Quadratic   -0.45614      0.09932     -4.5927          0
              Cubic    0.02919      0.00593     4.92296          0

      3   Intercept     1.6695      1.53075     1.09064    0.27548
             Linear   10.11827      1.73041     5.84733          0
          Quadratic   -3.70726      0.59886    -6.19052          0
              Cubic    0.53764      0.07968     6.74723          0
            Quartic   -0.02459      0.00358    -6.85989          0
-------------------------------------------------------------------
      1      sigma1    3.95795      0.05912    66.94911          0
      2      sigma2    4.11085      0.07232    56.84354          0
      3      sigma3    4.00173      0.10076    39.71375          0
-------------------------------------------------------------------
      1         pi1    0.45891      0.02837           0          0
      2         pi2    0.34901       0.0219   -12.49729          0
      3         pi3    0.19208      0.01802   -48.32612          0
-------------------------------------------------------------------
Likelihood : -14564.35
```

For the EM method we write Method = ”EM”.

```
R> # EM
R> solEM = trajeR(Y = data[,2:11], A = data[,12:21],
+                 degre = c(0,3,4),
+                 Model = "CNORM", Method = "EM",
```

```
+                 ssigma = FALSE, hessian = TRUE)
R> solEMs = trajeR(Y = data[,2:11], A = data[,12:21],
+                  degre = c(0,3,4),
+                  Model = "CNORM", Method = "EM",
+                  ssigma = TRUE, hessian = TRUE)
```

We summarize the results in the following table:

Different sigma				Same sigma			
SolL		SolEM		SolLs		SolEMs	
par.	sd	par.	sd	par.	sd	par.	sd
Beta 1							
7.04940	0.08442	7.04940	0.08356	7.05316	0.08551	7.05316	0.08479
Beta 2							
19.30454	0.65370	19.30454	0.60682	19.31467	0.60063	19.31467	0.59430
-0.09315	0.48451	-0.09315	0.45447	-0.08935	0.46105	-0.08935	0.44501
-0.45614	0.09932	-0.45614	0.09383	-0.45753	0.09708	-0.45753	0.09187
0.02919	0.00593	0.02919	0.00563	0.02927	0.00591	0.02927	0.00551
Beta 3							
1.66950	1.53075	1.66950	1.34917	1.66950	1.33560	1.66950	1.35545
10.11827	1.73041	10.11827	1.52068	10.11834	1.50493	10.11834	1.52775
-3.70726	0.59886	-3.70726	0.52667	-3.70726	0.52183	-3.70726	0.52912
0.53764	0.07968	0.53764	0.07038	0.53764	0.06983	0.53764	0.07071
-0.02459	0.00358	-0.02459	0.00318	-0.02459	0.00316	-0.02459	0.00320
Sigma							
3.95795	0.05912	3.95795	0.05919	4.02028	0.06931	4.02028	0.06143
4.11085	0.07232	4.11085	0.07048	4.02028	0.06931	4.02028	0.06687
4.00173	0.10076	4.00173	0.09153	4.02028	0.06931	4.02028	0.09258
Pi							
0.45891	0.02837	0.45891	0.02247	0.45978	0.02782	0.45978	0.02247
0.34901	0.02190	0.34901	0.02151	0.34814	0.02146	0.34814	0.02150
0.19208	0.01802	0.19208	0.03111	0.19207	0.01770	0.19207	0.03110

We see that the loglikelihood and EM methods give exactly the same parameter estimates, but the EM method is a little bit more precise in the sense that the standard deviations of the estimates are a little bit smaller for the EM algorithm.

Next, we add a risk variable influencing group membership to our model, by using the parameter `Risk`. For the likelihood method, the syntax of the command is

```
R> solLRisks = trajeR(Y = data[,2:11], A = data[,12:21], Risk =
data[,42:43], +                     degre = c(0,3,4), +
Model = "CNORM", Method = "L", +                    ssigma = TRUE,
hessian = TRUE)
```

In case of a common sigma for the whole population, we get

```
Model : Censored Normal
Method : Likelihood
```

```
  group   Parameter   Estimate   Std. Error   T for H0:    Prob>|T|
                                              param.=0
-------------------------------------------------------------------
      1   Intercept    7.05306      0.08474    83.23669           0

      2   Intercept   19.31517      0.58748    32.87782           0
             Linear   -0.09075      0.43826    -0.20707     0.83597
          Quadratic   -0.45723      0.09022    -5.06774           0
              Cubic    0.02926      0.00539     5.43167           0

      3   Intercept    1.66955      1.31776     1.26696     0.20523
             Linear   10.11834       1.4817     6.82887           0
          Quadratic   -3.70723      0.51392    -7.21361           0
              Cubic    0.53763      0.06885      7.8082           0
            Quartic   -0.02459      0.00312    -7.87674           0
-------------------------------------------------------------------
      1      sigma1    4.02025      0.06888    58.36946           0
      2      sigma2    4.02025      0.06888    58.36946           0
      3      sigma3    4.02025      0.06888    58.36946           0
-------------------------------------------------------------------
      1    Baseline          0           NA          NA          NA

      2   Intercept   -0.65904      0.27119    -2.43017     0.01513
                 X2    0.19531      0.35769     0.54604     0.58506
                 X3    0.57361      0.35407     1.62004     0.10529

      3   Intercept   -1.18428      0.31166     -3.7999     0.00015
                 X2     0.1063      0.41207     0.25796     0.79645
                 X3    0.52553      0.41243     1.27423     0.20264
-------------------------------------------------------------------
Likelihood : -14563.99
```

For the EM method, the syntax of the command is

```
R> solLRisks = trajeR(Y = data[,2:11], A = data[,12:21], Risk =
data[,42:43], +                    degre = c(0,3,4), + Model =
"CNORM", Method = "EM", +                      ssigma = TRUE,
hessian = TRUE)
```

We can summerize the different results in the following table:

Different sigma				Same sigma			
SolLRisk		SolEMRisk		SolLRisks		SolEMRisks	
par.	sd	par.	sd	par.	sd	par.	sd
Beta 1							
7.04923	0.08510	7.04923	0.08360	7.05306	0.08474	7.05306	0.08483
Beta 2							
19.30497	0.73763	19.30497	0.60687	19.31517	0.58748	19.31517	0.59428
-0.09451	0.56078	-0.09451	0.45450	-0.09075	0.43826	-0.09075	0.44498
-0.45584	0.11299	-0.45584	0.09383	-0.45723	0.09022	-0.45723	0.09186
0.02917	0.00658	0.02917	0.00563	0.02926	0.00539	0.02926	0.00551
Beta 3							
1.66955	1.41870	1.66955	1.34916	1.66955	1.31776	1.66955	1.35546
10.11828	1.59854	10.11828	1.52066	10.11834	1.48170	10.11834	1.52777
-3.70722	0.55243	-3.70722	0.52666	-3.70723	0.51392	-3.70723	0.52913
0.53763	0.07365	0.53763	0.07038	0.53763	0.06885	0.53763	0.07071
-0.02459	0.00332	-0.02459	0.00318	-0.02459	0.00312	-0.02459	0.00320
Sigma							
3.95767	0.05939	3.95767	0.05917	4.02025	0.06888	4.02025	0.06142
4.11119	0.06315	4.11119	0.07048	4.02025	0.06888	4.02025	0.06685
4.00162	0.09235	4.00162	0.09151	4.02025	0.06888	4.02025	0.09256
Theta - First group 0							
-0.65570	0.26496	-0.65570	0.26688	-0.65904	0.27119	-0.65904	0.26699
0.19567	0.35684	0.19567	0.35261	0.19531	0.35769	0.19531	0.35270
0.57547	0.35354	0.57547	0.34963	0.57361	0.35407	0.57361	0.34976
-1.18319	0.31079	-1.18319	0.32288	-1.18428	0.31166	-1.18428	0.32284
0.10679	0.40464	0.10679	0.42699	0.10630	0.41207	0.10630	0.42686
0.52683	0.39311	0.52683	0.42356	0.52553	0.41243	0.52553	0.42354

Finally, we add a time-dependent covariate by using the parameter `TCOV`. As before, we use the results of the basic finite mixture model as initial parameters. For the likelihood method, the correct syntax is

```
R> paraminit = c(solL$theta, solL$beta,solL$sigma, 0,0,0,0,0,0) R>
solLTCOV2 = trajeR(Y = data[,2:11], A = data[,12:21], TCOV =
data[,22:41], +                    degre = c(0,3,4), +
Model = "CNORM", Method = "L", +                    ssigma =
FALSE, hessian = TRUE)

R> solLTCOV2
```

The results are

```
Model : Censored Normal
Method : Likelihood

  group    Parameter    Estimate    Std. Error    T for H0:    Prob>|T|
                                                  param.=0
```

```
-----------------------------------------------------------------
      1   Intercept    6.75767      0.18877    35.79904          0
              TCOV1   -0.00356      0.16759    -0.02125    0.98305
              TCOV2    0.58131      0.28646     2.02928    0.04248

      2   Intercept   19.45638       0.6439    30.21642          0
             Linear   -0.09667      0.45288    -0.21345    0.83098
          Quadratic    -0.4549      0.09361    -4.85975          0
              Cubic    0.02909      0.00562     5.17774          0
              TCOV1   -0.17069      0.19963    -0.85502    0.39258
              TCOV2   -0.13292      0.34561    -0.38458    0.70056

      3   Intercept    1.81446      1.38383     1.31119    0.18985
             Linear   10.11476      1.52332     6.63996          0
          Quadratic   -3.70808        0.527     -7.0362          0
              Cubic    0.53803      0.07039     7.64322          0
            Quartic   -0.02462      0.00318    -7.73633          0
              TCOV1     0.0805      0.26198     0.30728    0.75865
              TCOV2   -0.35937      0.46289    -0.77636    0.43757
-----------------------------------------------------------------
      1      sigma1    3.95414      0.05924    66.74877          0
      2      sigma2    4.11016      0.07047    58.32808          0
      3      sigma3    4.00019      0.09155    43.69635          0
-----------------------------------------------------------------
      1         pi1    0.45879      0.02261           0          0
      2         pi2    0.34913      0.02149   -12.71034          0
      3         pi3    0.19208      0.01784   -48.80882          0
-----------------------------------------------------------------
Likelihood : -14561.48
```

To use the EM algorithm, with and without a constant value for σ he write

```
R> solEMTCOV2s = trajeR(Y = data[,2:11], A = data[,12:21], TCOV =
data[,22:41], +                       degre=c(0,3,4),
Model="CNORM", Method = "EM", +                       ssigma =
TRUE, hessian = TRUE)

R> solEMTCOV2 = trajeR(Y = data[,2:11], A = data[,12:21], TCOV =
data[,22:41], + degre=c(0,3,4), Model="CNORM", Method = "EM", +
ssigma = FALSE, hessian = TRUE)
```

The results are summarized in the following table:

Different sigma				Same sigma			
SolLTCOV2		SolEMTCOV2		SolLTCOV2s		SolEMTCOV2s	
par.	sd	par.	sd	par.	sd	par.	sd
Beta 1							
6.75767	0.18877	6.75768	0.18755	6.76379	0.19039	6.76375	0.19034
Beta 2							
19.45638	0.64390	19.45638	0.64707	19.46854	0.63556	19.46852	0.63333
-0.09667	0.45288	-0.09667	0.45490	-0.09328	0.44763	-0.09328	0.44524
-0.45490	0.09361	-0.45490	0.09391	-0.45624	0.09226	-0.45624	0.09191
0.02909	0.00562	0.02909	0.00563	0.02917	0.00552	0.02917	0.00551
Beta 3							
1.81446	1.38383	1.81446	1.37143	1.81446	1.35819	1.81446	1.37756
10.11476	1.52332	10.11476	1.52062	10.11485	1.50540	10.11485	1.52742
-3.70808	0.52700	-3.70808	0.52667	-3.70809	0.52211	-3.70809	0.52902
0.53803	0.07039	0.53803	0.07038	0.53803	0.06985	0.53803	0.07070
-0.02462	0.00318	-0.02462	0.00318	-0.02462	0.00316	-0.02462	0.00320
Sigma							
3.95414	0.05924	3.95414	0.05913	4.01801	0.06961	4.01801	0.06142
4.11016	0.07047	4.11016	0.07048	4.01801	0.06961	4.01801	0.06680
4.00019	0.09155	4.00019	0.09148	4.01801	0.06961	4.01801	0.09249
Delta 1							
-0.00356	0.16759	-0.00356	0.16624	-0.00763	0.16854	-0.00762	0.16875
0.58131	0.28646	0.58130	0.28559	0.58090	0.28994	0.58095	0.28982
Delta 2							
-0.17069	0.19963	-0.17069	0.19830	-0.16725	0.19367	-0.16724	0.19407
-0.13292	0.34561	-0.13291	0.34384	-0.13780	0.33793	-0.13777	0.33653
Delta 3							
0.08050	0.26198	0.08050	0.25900	0.08045	0.25954	0.08044	0.26016
-0.35937	0.46289	-0.35936	0.45630	-0.35932	0.45922	-0.35934	0.45834
Pi							
0.45879	0.02261	0.45879	0.03112	0.45970	0.02252	0.45970	0.03111
0.34913	0.02149	0.34913	0.02248	0.34823	0.02148	0.34823	0.02248
0.19208	0.01784	0.19208	0.02152	0.19207	0.01775	0.19207	0.02150

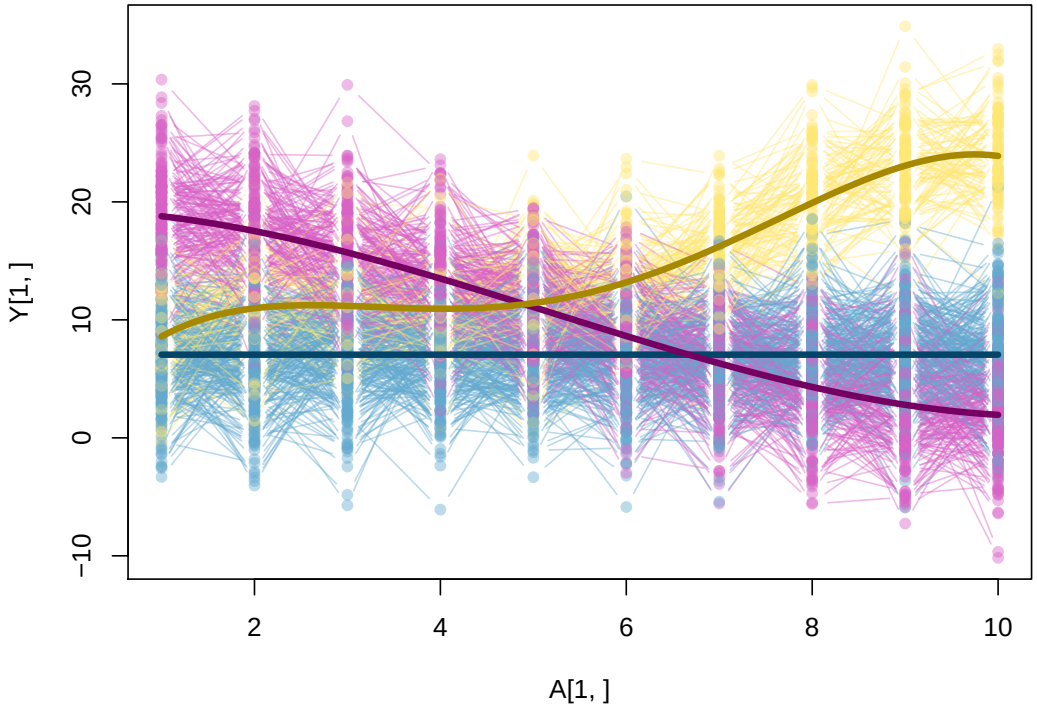
We see that the delta parameters are not significant for any of the three groups. This means that the time-dependent covariate W does actually not influence the trajectories.

5.2 Plots

We start by plotting the typical trajectories of each group for the basic finite mixture model, together with the initial trajectories of all individuals in the sample.

```
R> # colour's defintion
R> trans = "70"
R> col1 = "#034569"
```

```
R> col1.1 = paste0("#64AAD0", trans)
R> col2 = "#750062"
R> col2.1 = paste0("#D962C7", trans)
R> col3 = "#A68900"
R> col3.1 = paste0("#FFE773", trans)
R> cols1 = c(col1.1, col2.1, col3.1)
R> cols2 = c(col1, col2, col3)
R> vcol = c(cols1, cols2)
R>
R> plot(solEM, Y = data[,2:11], A = data[,12:21], col = vcol)
```

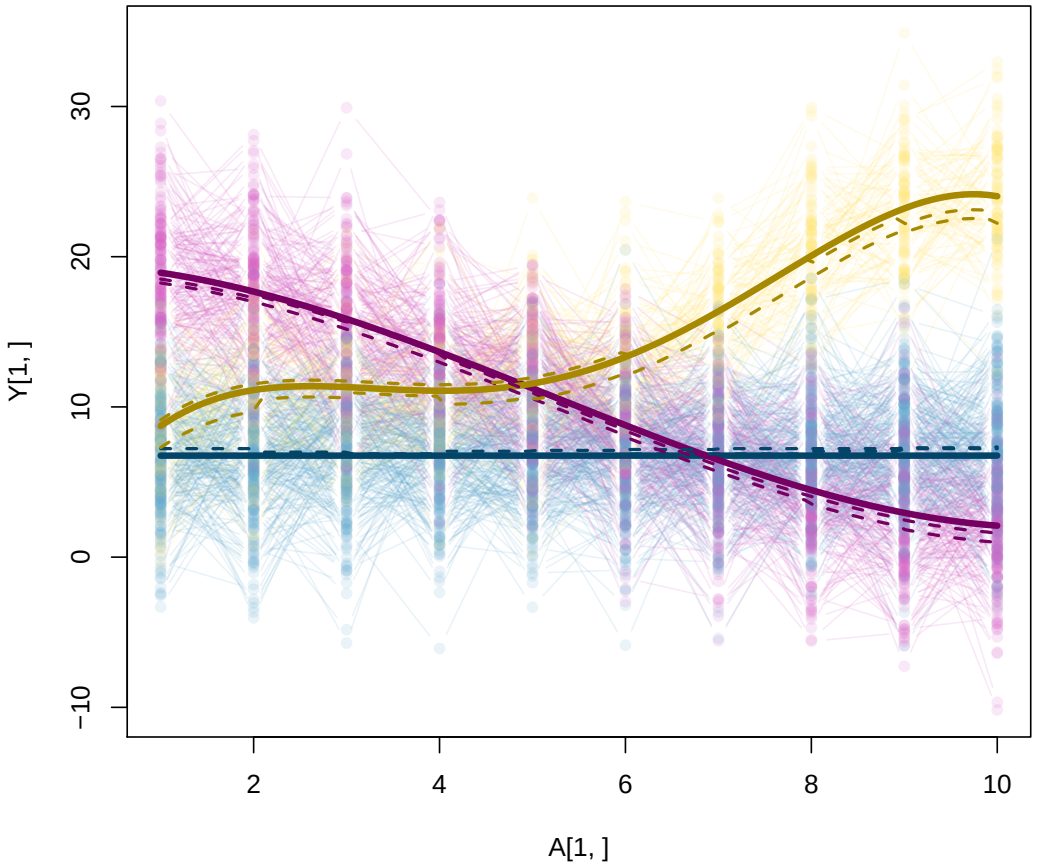


We can add the effect of a time covariate on the plot by using the option `plotcov` in the function `plot`. For example if we want see the effect of two different configurations of the time covariate, a first one with no impact of the first time covariate with 0 values for each time and for the second time covariate a strong impact for the first time value, decreasing around the value 5 then increasing again. And a second one, with full impact of the firt time covariate and an increasing effect for the second time covariate.

```
R> trans = "25" R> col1 = "#034569" R>
col1.1=paste0("#64AAD0",trans) R> col2 = "#750062" R> col2.1 =
paste0("#D962C7", trans) R> col3 ="#A68900" R> col3.1 =
```

```
paste0("#FFE773", trans) R> cols1 = c(col1.1, col2.1, col3.1) R>
cols2 = c(col1, col2, col3) R> vcol = c(cols1, cols2) R> plotcov =
c(c(rep(0,10), 0.8,0.4,0.2,0.5,0.6,0.7,0.8,0.8,0.9,1), +
c(rep(1,10), 0.,0.,0.,0.,0.,0.2,0.2,0.5,0.8,0.8))

R> plot(solLTCOV2, Y = data[,2:11], A = data[,12:21], col = vcol,
plotcov = plotcov)
```



6 Censored Data

In this section, we illustrate the difference between a model with underlying normal distribution and underlying censored normal distribution.

TrajeR allows to manually censor normal data by deciding on the lower and upper bound of the distribution. In the following example, we decide to changed all values larger than 23 into 23 and all values smaller than 2 into 2.
The correponding syntax for a likelihood method is

```
R> solLC = trajeR(Y = dataC[,2:11], A = dataC[,12:21],
+                 degre = c(0,3,4),
+                 Model="CNORM", Method = "L",
+                 ssigma = FALSE, hessian = TRUE,
+                 ymin=2, ymax=23)
```

The result is

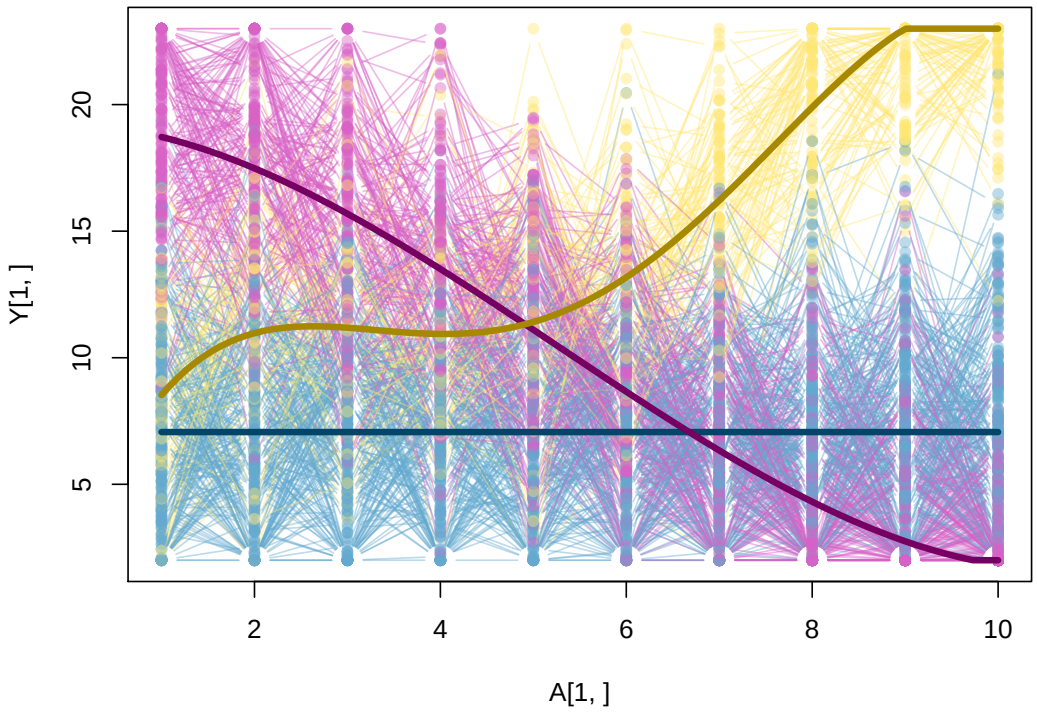
```
Model : Censored Normal
Method : Likelihood
```

group	Parameter	Estimate	Std. Error	T for H0: param.=0	Prob>|T|
1	Intercept	7.06352	0.08349	84.60614	0
2	Intercept	19.23116	0.62361	30.83834	0
	Linear	-0.08916	0.47328	-0.18839	0.85058
	Quadratic	-0.44929	0.09893	-4.54148	1e-05
	Cubic	0.02841	0.00599	4.74365	0
3	Intercept	1.47075	1.39933	1.05104	0.29329
	Linear	10.30212	1.58628	6.49453	0
	Quadratic	-3.7672	0.55383	-6.80215	0
	Cubic	0.54581	0.07468	7.30859	0
	Quartic	-0.02499	0.0034	-7.34021	0
1	sigma1	3.92236	0.06474	60.58621	0
2	sigma2	4.10491	0.08024	51.15891	0
3	sigma3	4.00573	0.10217	39.20749	0
1	pi1	0.45829	0.02795	0	0
2	pi2	0.34961	0.02151	-12.58569	0
3	pi3	0.1921	0.01786	-48.69404	0

```
Likelihood : -13317.83
```

We see on the graph, that trajectories that leave the bounds in case of a normal distribution become lines at the boundary in case of censored normal distributions.

```
R> plot(solLC, Y = dataC[,2:11], A = dataC[,12:21], col = vcol)
```

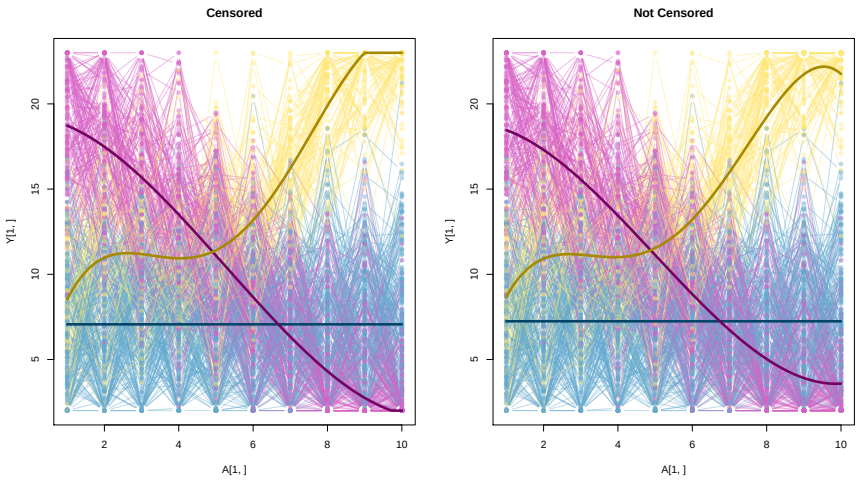


Calibrating the model without taking into account the real nature of the data leads to wrong parameter estimates. Treating a sample from a normal distribution as if it where censored data amounts to considering that the maximum and minimum of the sample are the theoretical bounds of the distribution. To illustrate this fact we compute the parameters of the previous example, without supposing that the data are censored. The result for the parameter estimates are shown in the following sample.

Censored	Not Censored
Beta 1	
7.0635200	7.2424800
Beta 2	
19.2311600	18.8466500
-0.0891600	0.0639900
-0.4492900	-0.4835500
0.0284100	0.0324500
Beta 3	
1.4707500	2.3253200
10.3021200	9.3139500
-3.7672000	-3.4181600
0.5458100	0.5013300
-0.0249900	-0.0233200
Sigma	
3.9223600	3.5980600
4.1049100	3.5482400
4.0057300	3.6012300
Pi	
0.4582880	0.4588787
0.3496098	0.3489176
0.1921022	0.1922037

The difference between the two situations can best be seen in the graphs below. On the left side, we have the typical trajectories in case of censored data, whereas on the right side, we see the typical trajectories for an underlying normal distribution that is not censored.

```
R> par(mfrow=c(1,2))
R> plot(solLC, Y = dataC[,2:11], A = dataC[,12:21], col = vcol, main="Censored")
R> plot(solLnC, Y = dataC[,2:11], A = dataC[,12:21], col = vcol, main="Not Censored" )
```



For censored normal data, we can of course also use the 3 methods to calibrate the model.

```
R> solLCs = trajeR(Y = dataC[,2:11], A = dataC[,12:21],
+                  degre = c(0,3,4),
+                  Model="CNORM", Method = "L",
+                  ssigma = TRUE, hessian = FALSE,
+                  ymin = 2,  ymax = 23)
R> solEMC = trajeR(Y = dataC[,2:11], A = dataC[,12:21],
+                  degre = c(0,3,4),
+                  Model="CNORM", Method = "EM",
+                  ssigma = FALSE, hessian = FALSE,
+                  ymin = 2,  ymax = 23)
R> solEMCs = trajeR(Y = dataC[,2:11], A = dataC[,12:21],
+                   degre = c(0,3,4),
+                   Model="CNORM", Method = "EM",
+                   ssigma = TRUE, hessian = FALSE,
+                   ymin = 2,  ymax = 23)
```

Different sigma				Same sigma			
SolLC		SolEMC		SolLCs		SolEMCs	
par.	sd	par.	sd	par.	sd	par.	sd
Beta 1							
7.06352	0.08349	7.06352	0.08300	7.06261	0.08420	7.06261	0.08455
Beta 2							
19.23116	0.62361	19.23116	0.60570	19.23109	0.59354	19.23109	0.59103
-0.08916	0.47328	-0.08916	0.45345	-0.08164	0.44977	-0.08164	0.44246
-0.44929	0.09893	-0.44929	0.09359	-0.45135	0.09405	-0.45135	0.09132
0.02841	0.00599	0.02841	0.00561	0.02859	0.00569	0.02859	0.00548
Beta 3							
1.47075	1.39933	1.47075	1.35126	1.47257	1.34574	1.47257	1.34916
10.30212	1.58628	10.30213	1.52307	10.30028	1.52141	10.30028	1.52071
-3.76720	0.55383	-3.76720	0.52752	-3.76648	0.53048	-3.76648	0.52670
0.54581	0.07468	0.54581	0.07049	0.54571	0.07139	0.54571	0.07038
-0.02499	0.00340	-0.02499	0.00319	-0.02498	0.00325	-0.02498	0.00318
Sigma							
3.92236	0.06474	3.92236	0.06729	3.99933	0.07665	3.99933	0.07061
4.10491	0.08024	4.10491	0.09013	3.99933	0.07665	3.99933	0.08410
4.00573	0.10217	4.00573	0.11011	3.99933	0.07665	3.99933	0.10960
Pi							
0.45829	0.02795	0.45829	0.02247	0.45937	0.02761	0.45937	0.02247
0.34961	0.02151	0.34961	0.02152	0.34855	0.02138	0.34855	0.02150
0.19210	0.01786	0.19210	0.03111	0.19208	0.01747	0.19208	0.03110

And finally, adding time-dependent covariates works in the following way.

```
R> solLCTCOV = trajeR(Y = dataC[,2:11], A = dataC[,12:21], TCOV = dataC[,22:31],
+                     degre = c(0,3,4),
```

```
+                     Model = "CNORM", Method = "L",
+                     ssigma = FALSE, hessian = FALSE,
+                     ymin = 2,  ymax = 23)
R> solLCTCOVs = trajeR(Y = dataC[,2:11], A = dataC[,12:21], TCOV = dataC[,22:31],
+                       degre = c(0,3,4),
+                       Model = "CNORM", Method = "L",
+                       ssigma = TRUE, hessian = FALSE,
+                       ymin = 2,  ymax = 23)
R> solEMCTCOV = trajeR(Y = dataC[,2:11], A = dataC[,12:21], TCOV = dataC[,22:31],
+                       degre = c(0,3,4),
+                       Model = "CNORM", Method = "EM",
+                       ssigma = TRUE, hessian = FALSE,
+                       ymin = 2,  ymax = 23)
R> solEMCTCOVs = trajeR(Y = dataC[,2:11], A = dataC[,12:21], TCOV = dataC[,22:31],
+                        degre = c(0,3,4),
+                        Model = "CNORM", Method = "EM",
+                        ssigma = FALSE, hessian = FALSE,
+                        ymin = 2,  ymax = 23)
```

Different sigma				Same sigma			
SolLCTCOV		SolEMCTCOV		SolLCTCOVs		SolEMCTCOVs	
par.	sd	par.	sd	par.	sd	par.	sd
Beta 1							
7.05899	0.11872	7.05899	0.11719	7.06103	0.12740	7.06103	0.11940
Beta 2							
19.32126	0.63461	19.32125	0.61168	19.31862	0.61585	19.31862	0.59683
-0.08347	0.47521	-0.08347	0.45331	-0.07567	0.45384	-0.07567	0.44232
-0.44993	0.09884	-0.44993	0.09357	-0.45206	0.09332	-0.45206	0.09130
0.02843	0.00597	0.02843	0.00561	0.02861	0.00561	0.02861	0.00548
Beta 3							
1.41793	1.34024	1.41793	1.35507	1.41982	1.37305	1.41982	1.35296
10.27971	1.50236	10.27971	1.52330	10.27787	1.54889	10.27787	1.52094
-3.75951	0.52252	-3.75951	0.52759	-3.75879	0.53883	-3.75879	0.52677
0.54480	0.07030	0.54480	0.07050	0.54470	0.07245	0.54470	0.07039
-0.02494	0.00320	-0.02494	0.00319	-0.02494	0.00330	-0.02494	0.00318
Sigma							
3.92171	0.06409	3.92171	0.06730	3.99871	0.07574	3.99871	0.07061
4.10429	0.07937	4.10429	0.09011	3.99871	0.07574	3.99871	0.08408
4.00512	0.10448	4.00512	0.11010	3.99871	0.07574	3.99871	0.10959
Delta 1							
0.00793	0.16942	0.00793	0.16495	0.00200	0.17241	0.00200	0.16798
Delta 2							
-0.20534	0.21333	-0.20533	0.19771	-0.20032	0.19041	-0.20032	0.19288
Delta 3							
0.13640	0.28471	0.13640	0.25929	0.13626	0.26325	0.13626	0.25889
Pi							
0.45818	0.02252	0.45818	0.03111	0.45927	0.02218	0.45927	0.03110
0.34971	0.02164	0.34971	0.02247	0.34864	0.02166	0.34864	0.02247
0.19210	0.01766	0.19210	0.02152	0.19209	0.01722	0.19209	0.02150

7 The Zero Inflated Poisson model

The ZIP (Zero Inflated Poisson) model consists of two seperate distributions : a binary distribution that generates structural zeros, i.e. the excess zeros, and a Poisson distribution that generates the counts.

In this model, a value of zero can occur for two reasons. First, the count can be equal to zero (with a probability $P(Z_{it} = 0)$ for $Z_{it} \sim \mathcal{P}(\lambda_{ikt})$ and second the binary distribution can be zero (with a probability ρ_{ikt}).

We have

$$P\left(Y_{it} = y_{it} | W_i = wi, C_i = ci\right) = \begin{cases} \rho_{ikt} + (1-\rho_{ikt})e^{-\lambda_{ikt}}, & y_{it} = 0 \\ (1-\rho_{ikt})\frac{\lambda_{ikt}^{y_{it}} e^{-\lambda_{ikt}}}{y_{it}!}, & y_{it} > 0 \end{cases} . \tag{16}$$

The link functions λ_k and ρ_k that connect the developmental trajectory with age are given by

$$\log(\lambda_{ikt}) = \beta_k A_{it} + \delta_k W_t \tag{17}$$

and ρ_{ikt}

$$\log\left(\frac{\rho_{ikt}}{1-\rho_{ikt}}\right) = \nu_k A_{it}, \tag{18}$$

where $A_{it} = (1, a_{it}, a_{it}^2, \cdots, a_{it}^{n_\beta - 1})^t$, $W_t = (w_{i1}, \cdots, w_{in_\delta})^t$, $\beta_k = (\beta_{k1}, \cdots, \beta_{kn_\beta})$ and $\delta_k = (\delta_{k1}, \cdots, \delta_{kn_\delta})$.

Thus,

$$g_k(y_i; \beta_k, \delta_k) = \prod_{y_{it}=0} \left(\rho_{ikt} + (1-\rho_{ikt})e^{-\lambda_{ikt}}\right) \prod_{y_{it}>0} (1-\rho_{ikt}) \frac{\lambda_{ikt}^{y_{it}} e^{-\lambda_{ikt}}}{y_{it}!}$$

and the log likelihood is given by

$$l(\psi; y) = \sum_{i=1}^{n} \log\left(\sum_{k=1}^{K} \pi_k \prod_{y_{it}=0} \left(\rho_{ikt} + (1-\rho_{ikt})e^{-\lambda_{ikt}}\right) \prod_{y_{it}>0} (1-\rho_{ikt}) \frac{\lambda_{ikt}^{y_{it}} e^{-\lambda_{ikt}}}{y_{it}!}\right). \tag{19}$$

The output of the trajeR function is an object of class trajectory.ZIP that is constituted by a list containing at least the following components:

Parameters	Description
beta	a vector with the beta parameters.
delta	a vector with the delta parameters (only exists in case of a covariate function W).
theta	a vector with the theta parameters (only exists in case of a covariate function X).
nu	a vector with the nu parameters
sd	a vector with the standard deviations of the estimated parameters.
tab	a matrix with all estimated parameters and their standard deviations.
model	a string stating which model was used.
groups	an integer giving the number of groups.
Names	the names of the beta parameters (intercept, linear, quadratic...)
Method	a string stating which method was used.
Size	an integer giving the sample size.
Likelihood	a real number giving the likelihood of the model.
Time	a vector with the time points ie the first line of matrix A.
degre	a vector with the degrees of the typical polynomial trajectories in the different groups.
degre.nu	a vector with the degree of the polynomial shape for the exceeded zero state.

7.1 Simulation example

We use the simulated dataset ZIP_data01 that comes with installing the package from the CRAN repository. The sample consists of 500 trajectories with 5 time-points each. The dataset

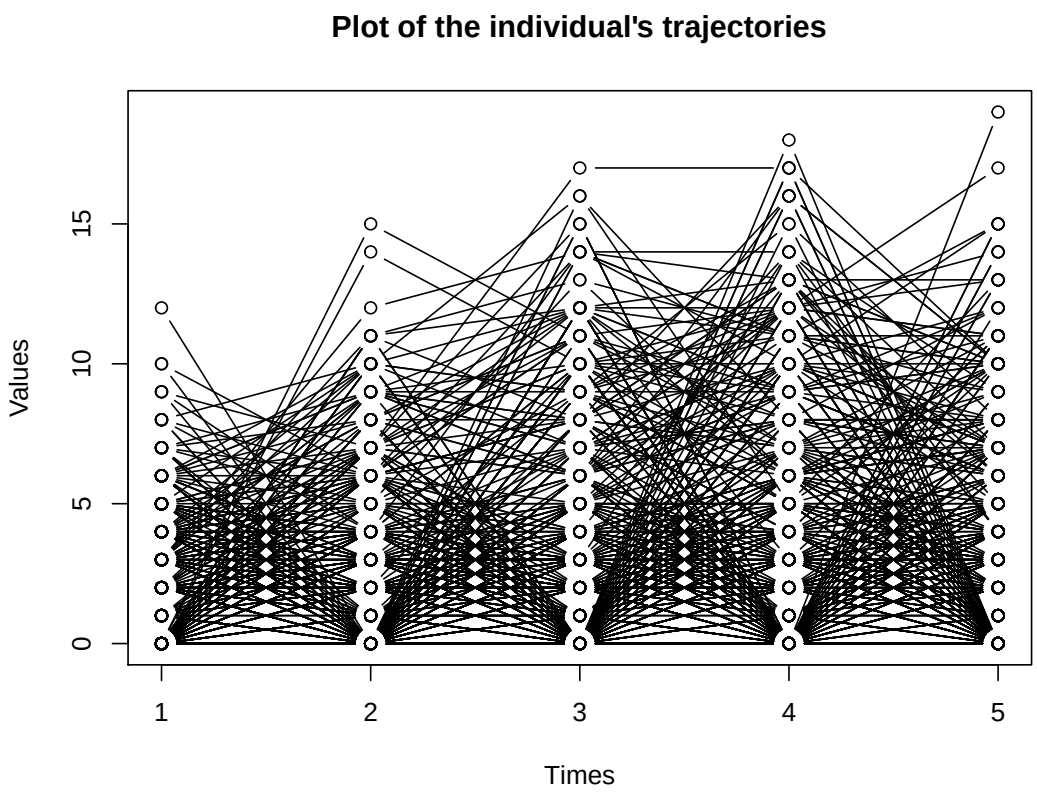
is split into 2 groups. For group 1, the degree in the Poisson state is 2 with parameters $\beta_1 = (1.2, 0.5, -0.06)$ and for the zero state the degree is 1 with parameter $\nu_1 = (-0.2, -0.1)$. For group 2, the degree in the Poisson state is 2 with parameters $\beta_2 = (0.89, 0.01, 0.01)$ and for the zero state the degree is 1 with parameter $\nu_2 = (-1, 0)$. The parameters are summarized in the table

Parameters	β_{k0}	β_{k1}	β_{k2}	ν_{k1}	ν_{k2}	π_k
Group 1	1.2	0.5	-0.06	-0.2	-0.1	0.3
Group 2	0.89	0.01	0.01	-1	0	0.7

The variable of interest Y is stored in `dataZIP[,2:6]`, the time variable in `dataZIP[,7:11]`, the time-dependent covariate W in `dataZIP[,13:17]` and a covariate X that influences group membership in `dataZIP[,12]`. Hence,

`data[,2:6]`	is a matrix with real numbers.
`data[,7:11]`	is a matrix with integers from 1 to 5.
`data[,13:17]`	is a matrix with values 0 and 1 value.
`data[,12]`	is a matrix with real numbers.

First we plot the data to get a first impression.



We fit the model with the two methods. We choose a 2-group solution by putting 2 values in the degre and degre.nu parameters

We specify `hessian=TRUE` in order to compute the Hessian matrix.

For the Likelihood method we use `trajeR` with parameter `Method ="L"`.

```
R> # Likelihood
R> solL = trajeR(Y = data[,2:6], A = data[,7:11],
+                degre=c(2,2), degre.nu = c(1,1),
+                Model="ZIP", Method = "L", hessian = TRUE)


Model : Zero Inflated Poisson
Method : Likelihood

  group   Parameter   Estimate   Std. Error   T for H0:   Prob>|T|
                                              param.=0
-----------------------------------------------------------------------
      1   Intercept    0.90782      0.09682     9.37679          0
             Linear    0.01872      0.07173     0.26104    0.79408
          Quadratic    0.00618      0.01157     0.53465    0.59294
               Nu11   -1.08146      0.16213    -6.67048          0
               Nu12    0.00454      0.04803     0.09451    0.92471

      2   Intercept    1.04873      0.09571    10.95765          0
             Linear    0.61507      0.06511     9.44664          0
          Quadratic   -0.07773      0.01009    -7.70501          0
               Nu21    0.03162      0.16834     0.18783    0.85102
               Nu22   -0.16776      0.05205    -3.22309    0.00128
-----------------------------------------------------------------------
      1         pi1    0.65132      0.02268           0          0
      2         pi2    0.34868      0.02268    -27.5523          0
-----------------------------------------------------------------------
Likelihood : -5162.009
```

For the EM method, we assign `EM` or `EMIRLS` to the parameter `Method`.

```
R> # EM
R> solEM = trajeR(Y = data[,2:6], A = data[,7:11],
+                 degre=c(2,2), degre.nu = c(1,1),
+                 Model="ZIP", Method = "EM", hessian = TRUE)
R> solEMIRLS = trajeR(Y = data[,2:6], A = data[,7:11],
+                     degre=c(2,2), degre.nu = c(1,1),
+                     Model="ZIP", Method = "EMIRLS", hessian = TRUE)
```

The results are summarized in the following table:

SolL		SolEM		SolEMIRLS	
parameters	sd	parameters	sd	parameters	sd
Beta 1					
0.90782	0.09682	0.90738	0.07865	0.90782	0.07864
0.01872	0.07173	0.01899	0.05853	0.01872	0.05853
0.00618	0.01157	0.00615	0.00947	0.00618	0.00947
Beta 2					
1.04873	0.09571	1.04879	0.07417	1.04873	0.07417
0.61507	0.06511	0.61503	0.04979	0.61507	0.04979
-0.07773	0.01009	-0.07773	0.00769	-0.07773	0.00769
Nu 1					
-1.08146	0.16213	-1.08166	0.16536	-1.08146	0.16534
0.00454	0.04803	0.00459	0.04874	0.00454	0.04874
Nu 2					
0.03162	0.16834	0.03160	0.18424	0.03162	0.18424
-0.16776	0.05205	-0.16775	0.05663	-0.16776	0.05663
Pi					
0.65132	0.02268	0.65132	0.02151	0.65132	0.02151
0.34868	0.02268	0.34868	0.02151	0.34868	0.02151

The syntax for adding a time-dependent covariate influencing the trajectories is the same than before. We again have the choice between the usual 3 methods.

```
R> solLTCOV = trajeR(Y = data[,2:6], A = data[,7:11], TCOV =
data[,13:17], +                    degre=c(2,2), degre.nu = c(1,1),
+                   Model="ZIP", Method = "L", hessian = TRUE)

R> solEMTCOV = trajeR(Y = data[,2:6], A = data[,7:11], TCOV =
data[,13:17], +                     degre=c(2,2), degre.nu =
c(1,1), itermax = 500, +                      Model="ZIP", Method =
"EM", hessian = TRUE)

R> solEMIRLSTCOV = trajeR(Y = data[,2:6], A = data[,7:11], TCOV =
data[,13:17], + degre=c(2,2), degre.nu = c(1,1), itermax = 500, +
Model="ZIP", Method = "EMIRLS", hessian = TRUE)
```

The results are summarized in the following table:

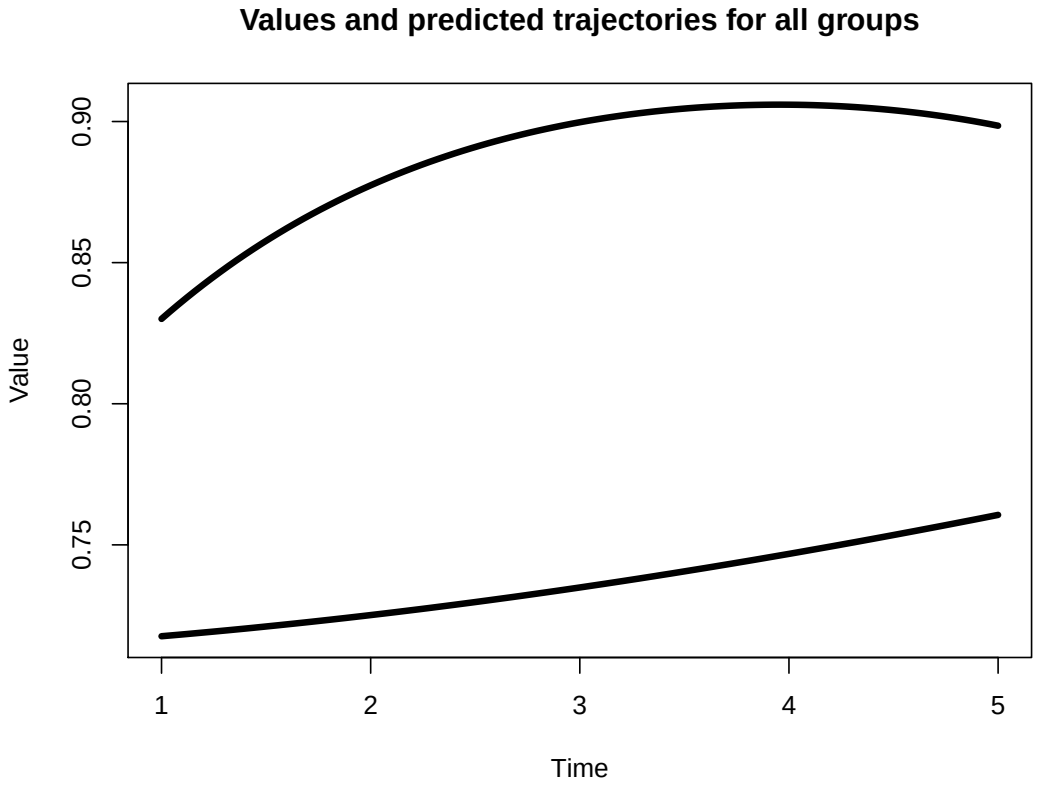
SolLTCOV		SolEMTCOV		SolEMIRLSTCOV	
par.	sd	par.	sd	par.	sd
Beta 1					
0.88074	0.10032	0.88036	0.08022	0.88074	0.08022
0.01538	0.07234	0.01557	0.05851	0.01538	0.05851
0.00677	0.01171	0.00674	0.00947	0.00677	0.00947
Beta 2					
1.04295	0.09688	1.04260	0.07501	1.04295	0.07500
0.61469	0.06573	0.61492	0.04963	0.61469	0.04963
-0.07767	0.01021	-0.07770	0.00767	-0.07767	0.00767
Nu 1					
-1.07079	0.15832	-1.07098	0.16464	-1.07079	0.16463
0.00234	0.04563	0.00238	0.04861	0.00234	0.04860
Nu 2					
0.02789	0.16772	0.02785	0.18501	0.02789	0.18501
-0.16707	0.05278	-0.16706	0.05686	-0.16707	0.05686
TCOV					
0.06375	0.04011	0.06381	0.03164	0.06375	0.03164
0.01297	0.03340	0.01299	0.02361	0.01297	0.02361
Pi					
0.65198	0.02298	0.65197	0.02151	0.65198	0.02151
0.34802	0.02298	0.34803	0.02151	0.34802	0.02151

We can add the effect of other time covariate.

7.2 Plots

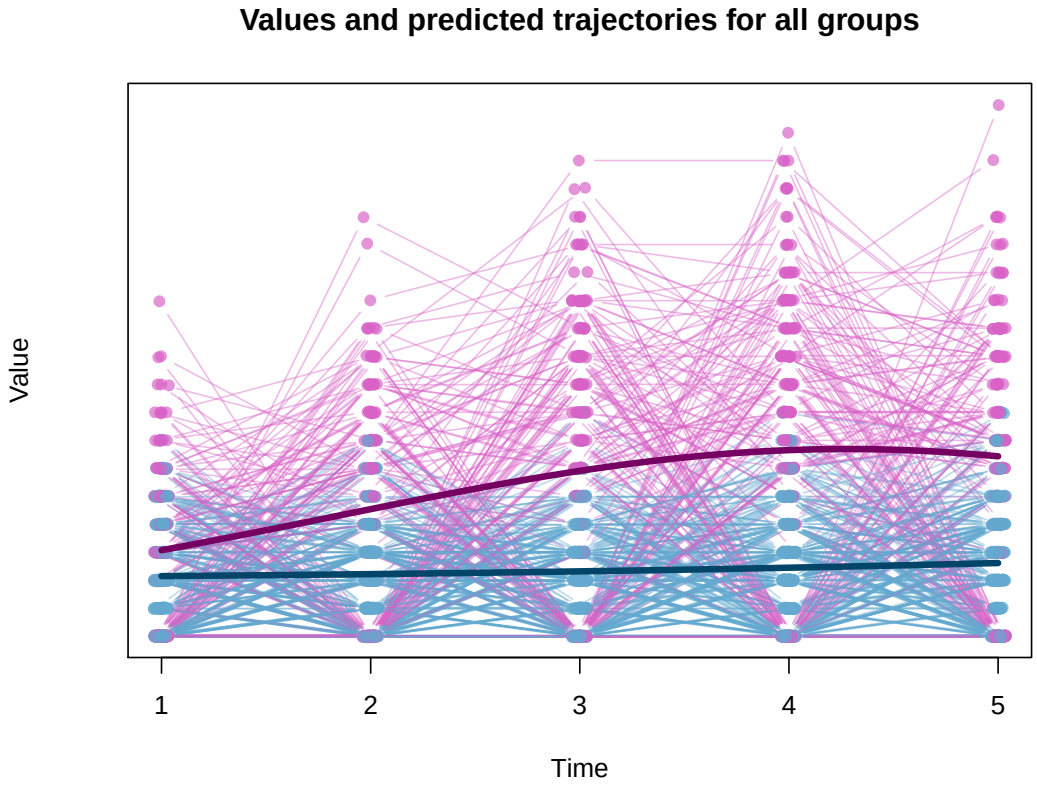
The typical trajectories of the 2 groups are plotted by

```
R> plot(solL)
```



We can also add the individual trajectories to the graph with different colors for the 2 groups.

```
R> # colour's defintion
R> trans = "70"
R> col1 = "#034569"
R> col1.1 = paste0("#64AAD0", trans)
R> col2 = "#750062"
R> col2.1 = paste0("#D962C7", trans)
R> cols1 = c(col1.1, col2.1)
R> cols2 = c(col1, col2)
R> vcol = c(cols1, cols2)
R>
R> plot(solEM, Y = dataZIP[,2:6], A = dataZIP[,7:11], dec = 4, col = vcol)
```



8 Nonlinear trajectories for the normal distribution

We suppose that the variable Y_{it} is defined by

$$y_{it} = f(a_{it}; \beta_k) + \varepsilon_{it}, \tag{20}$$

where $\varepsilon_{it} \sim \mathcal{N}(0;\ \sigma_k)$.

Here, the function f can be any funciton depending on some parameters β_k and

$$E(Y_{it} = y_{it} | W_i = w_i, Gi = k) = f(a_{it}; \beta_k). \tag{21}$$

Moreover,

$$P(Y_{it} = y_{it} | W_i = w_i, Gi = k) = \frac{1}{\sigma_k} \phi \left(\frac{y_{it} - f(a_{it}; \beta_k)}{\sigma_k} \right). \tag{22}$$

Thus,

$$g_k(y_i; \beta_k) = \prod_{t=1}^{T} \frac{1}{\sigma_k} \phi \left(\frac{y_{it} - \mu_{ikt}}{\sigma_k} \right) \tag{23}$$

and

$$l(\psi; y) = \sum_{i=1}^{n} \log \left(\sum_{k=1}^{K} \pi_k \prod_{t=1}^{T} \frac{1}{\sigma_k} \phi \left(\frac{y_{it} - \mu_{ikt}}{\sigma_k} \right) . \right) \tag{24}$$

To estimate the parameters we use the EM algorithm and the Levenberg Marquardt method.

8.1 Simulation example

We use the simulated dataset DataNonLinear01 that comes with installing the package from the CRAN repository. The sample consists of 500 trajectories with 10 time-points each. For the typical group trajectories, we consider the nonlinear function

$$f(t; \beta_k) = \frac{\beta_k t}{\beta_k + t}.$$

The dataset consists in a simulated 4 group solution, the parameters[1] of which are summarized in the following table

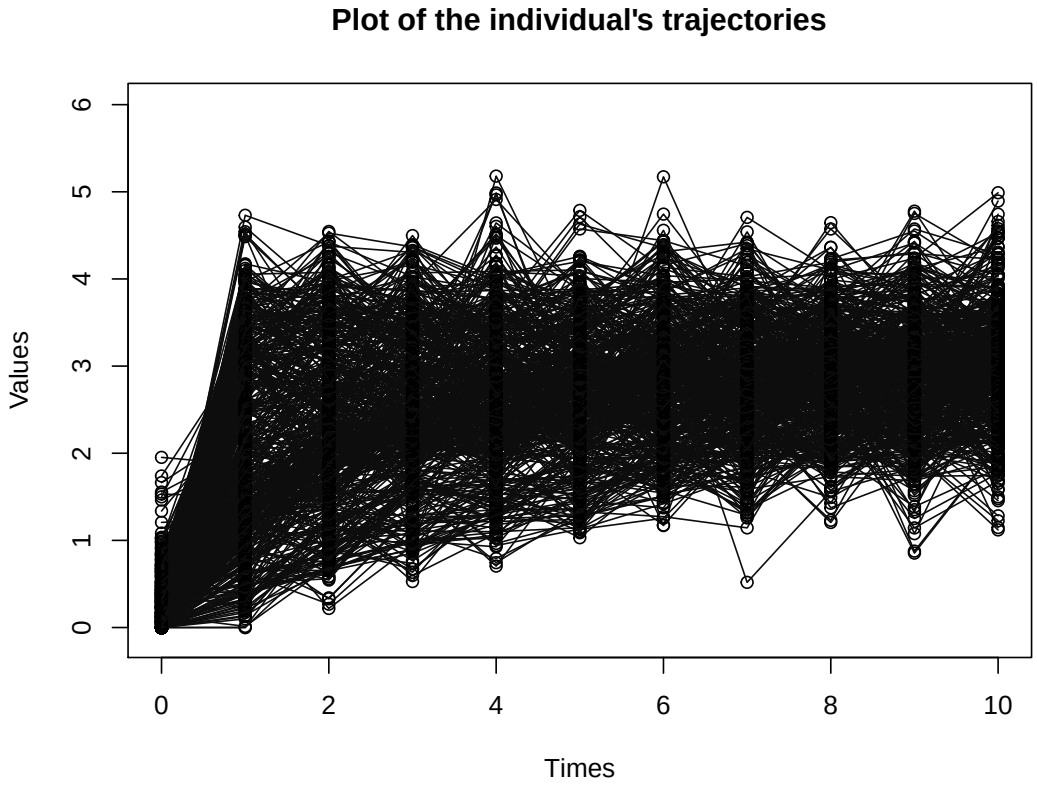
Parameters	β_{k1}	β_{k2}	π_k	σ_k
Group 1	3.6	0.025	0.45	0.2
Group 2	2.9	0.06	0.65	0.3
Group 3	3.4	5	0.35	0.14
Group 4	3.4	1.5	0.4	0.36

The variable of interest Y is stored in Y_i in `data[,2:12]`, the time variable in `data[,13:23]`. Hence,

`data[,2:12]`	is a matrix with real numbers.
`data[,13:23]`	is a matrix with integers from 0 to 10.

First we plot the data in order to get a first impression.

[1] the informed reader will have recognized, in order, *Glutamate dehydrogenase* in NAD^+, *Pyruvate carboxylaste* in ATP, *Threonine deaminase* in Threonine and *Hexokinase* in Fructose.



We use the EM algorithm to fit the model. We specify the number of group `ng.nl` to 4 and the number of parameters `nbvar` to 2.
`itermax` is set to 300 to assure a good approximation of the parameters.
After analyzing the graph above, we fix the initial parameters to

```
R> paraminit=c(0.25,0.25,0.25,0.25,2,0.1,2.4,0.1,2.8,0.1,3,0.1,0.2,0.2,0.2,0.2)
```

Then we have to define the function f and its differential.

```
R> #defintion of the function
R> fct <- function(t, betak, TCOV){
+   return(
+     (betak[1]*t)/(betak[2]+t)
+   )
+ }
R> #defintion of the differential
R> diffct <- function(t, betak, TCOV){
+   return(c(
+     t/(betak[2]+t),
+     -(betak[1]*t)/(betak[2]+t)**2
+   ))
+ }
```

Finally, we call `trajeR` with parameters `Method ="EM"` and `Model="NL"`.

```
R> solEM = trajeR(Y = data[,2:12], A = data[,13:23],
+                 ng.nl = 4, nbvar = 2,
+                 Method = "EM", Model = "NL", hessian = TRUE,
+                 fct = fct, diffct = diffct, paraminit = paraminit)
```

The results are given in the following table:

```
Model : Non Linear
Method : Expectation-maximization
```

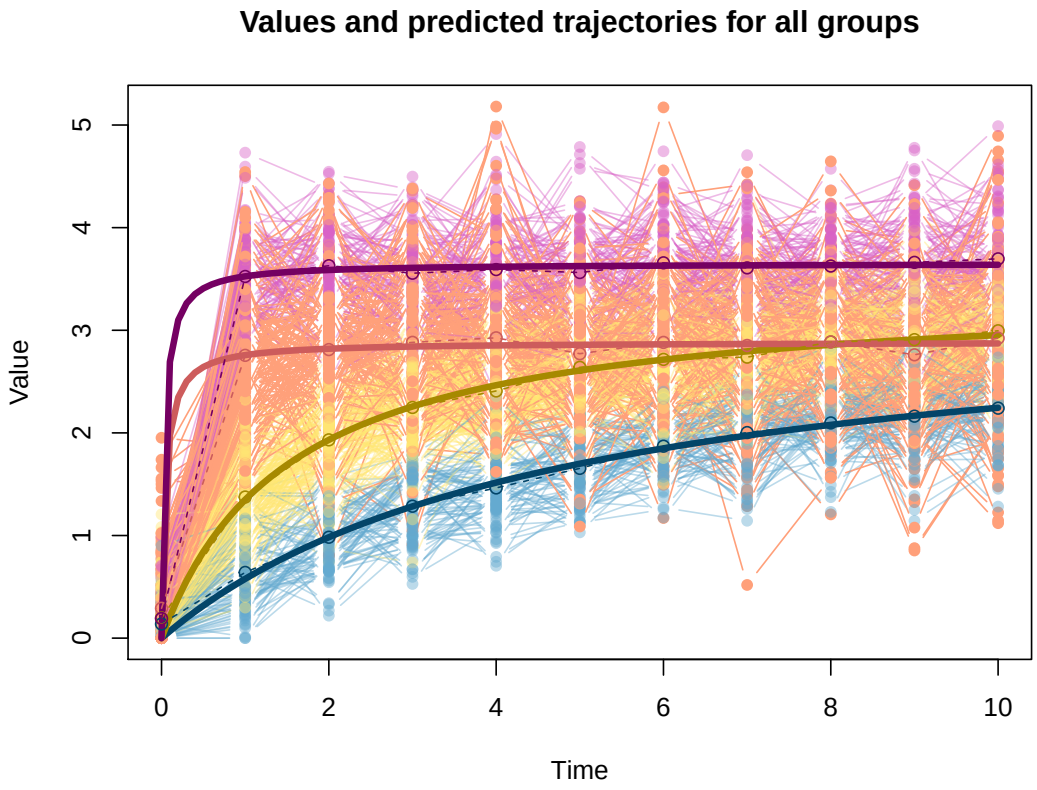
group	Parameter	Estimate	Std. Error	T for H0: param.=0	Prob>|T|
1	Intercept	3.30547	0.1011	32.69401	0
	Linear	4.72453	0.33069	14.28672	0
2	Intercept	3.40216	0.03124	108.89768	0
	Linear	1.52195	0.05773	26.36144	0
3	Intercept	2.88488	0.02606	110.68252	0
	Linear	0.04596	0.02516	1.82655	0.06782
4	Intercept	3.65116	0.02378	153.51625	0
	Linear	0.03562	0.01685	2.11433	0.03453
1	sigma1	0.34668	0.00842	41.1552	0
2	sigma2	0.39863	0.00725	54.95507	0
3	sigma3	0.64933	0.01147	56.62683	0
4	sigma4	0.43922	0.01037	42.34672	0
1	pi1	0.154	0.01611	9.55748	0
2	pi2	0.36068	0.02219	16.25187	0
3	pi3	0.31142	0.02135	14.58402	0
4	pi4	0.1739	0.03476	5.00316	0

```
Likelihood : -4209.639
```

We plot the graph with all individual trajectories, the typical group trajectories as well as the average trajectories for each group.

```
R> trans = "70"
R> col1 = "#034569"
R> col1.1 = paste0("#64AAD0", trans)
R> col2 = "#750062"
R> col2.1 = paste0("#D962C7", trans)
R> col3 = "#A68900"
R> col3.1 = paste0("#FFE773", trans)
R> col4 = "#CD5C5C"
```

```
R> col4.1 = "#FFA07A"
R> cols1 = c(col1.1, col3.1, col4.1, col2.1)
R> cols2 = c(col1, col3, col4, col2)
R> vcol = c(cols1, cols2)
R> plot(solEM, Y=data[,2:12], A=data[,13:23],col = vcol, mean = TRUE)
```



9 Group membership probabilities

It is usually very important in practice to know the group membership probabilities for all individuals in the sample. The command `GroupProb` allows to compute this. The output is a matrix of real numbers.
We illustrate this command with the results of page 22. The variable of interest Y was stored in data[,2:11], whereas the time variable was in data[,12:21]. To get the group membership probabilities of the first 8 individuals of our sample, we write

```
R> prob = GroupProb(solLs, Y =  data[,2:11], A = data[,12:21])
R> head(prob, n = 8)
```

The output is

```
              Gr1          Gr2          Gr3
[1,] 1.000000e+00 1.799942e-08 1.781949e-15
[2,] 1.931701e-07 2.276161e-16 9.999998e-01
[3,] 1.000000e+00 2.205456e-09 2.589024e-15
[4,] 1.000000e+00 2.869033e-08 6.055145e-16
[5,] 1.826708e-11 2.047939e-20 1.000000e+00
[6,] 9.999999e-01 1.116282e-07 2.165813e-13
[7,] 9.999998e-01 1.939171e-07 9.620129e-16
[8,] 9.988099e-01 1.190115e-03 6.048904e-11
```

So we see that subjects 1, 3, 4, 6, 7 and 8 are almost surely in group 1, whereas subjects 2 and 5 belong almost surely to group 3.

10 Group profiles

One interesting aspect of a model with covariates is the possibility to better understand the composition of the different groups by analyzing the average of the covariates in the different groups and compare them to their sample averages. These group profiles can be done using the function `GroupProfiles`. As an example,the syntax for getting group profiles for the 2 covariates stored in columns 42 and 43 of the matrix data, is

```
R> GroupProfiles(solLRisk, Y =  data[,2:11], A = data[,12:21], X = data[, 42:43])

          Gr 1      Gr 2      Gr 3
[1,] 0.4924891 0.5075429 0.5009375
[2,] 0.4700437 0.5187429 0.5144792
```

We see that V42 has quite similar values in the 3 groups, whereas V43 has a slightly lower average in group 1 than in the 2 other groups.

11 Model selection criteria

The criteria usually used for model selection in finite mixture models are the Bayesian Information Criterion (BIC) and the Akaike Information Criterion (AIC). These 2 classical criteria are implemented in trajeR, as well as the Slope Heuristic criterion.

```
R> trajeRBIC(solLRisk)

[1] 29255.68

R> trajeRAIC(solLRisk)

[1] 29167.18
```

`trajeRSH` need a list with a least 10 objects of type trajectory to work. Ajouter exemple d'application!

12 Model adequacy criteria

The posterior probabilities of group membership are among other a source of valuable information for judging the model's correspondence with the data (Nagin, 2005). We implemented the four diagnostics proposed in Nagin (2005) in trajeR.

Average Posterior Probability of Assignment

We call Average Posterior Probability of Assignment (AvePP) the average posterior probability of membership for each group for those individuals that were assigned to it. In a ideal situation the assignment probability for each individual would be 1 and the Average Posterior Probability (AvePP) would be 1 too. In our simulated example, we get

```
R> AvePP(solLRisk, Y = data[,2:11], A = data[,12:21], X = data[, 42:43])

[1] 0.9957065 0.9920113 0.9999998
```

We can see that all values are very close to 1. It means that the model fits the data correctly, which is of course not astonishing since the data were simulated to fit the model.

Odds of Correct Classification

The Odds of Correct Classification for group k ($\mathrm{OCC_k}$) is the ratio between the odds of a correct classification into group k on the basis of the posterior probability rule and the odds of correct assignment based on random assignments with the probability of assignment to group k is done with $\hat{\pi_k}$, the probability estimated by the model. Large values of OCC_k indicate a good assignment accuracy. Nagin suggests that in a real world application an OCC_k greater than 5 for all groups is indicative that the model has a high assigment accuracy (Nagin, 2005).

```
R> OCC(solL, Y = data[,2:11], A = data[,12:21])

[1] 2.767407e+02 2.270867e+02 2.532774e+07
```

Estimated Group Probabilities versus the Proportion of the Sample Assigned to the Group

We compute the probability of group membership by two methods : using $\hat{\pi_k}$ or using the proportion P_k of the sample assigned to the group k. Ideally the these two values should be equal.

```
R> propAssign(solL, Y =data[,2:11], A = data[,12:21])

gr
    1     2     3
0.458 0.350 0.192
```

We can compare with $\hat{\pi_k}$ ca calculate by the model.

```
R> exp(solL$theta)/sum(exp(solL$theta))

[1] 0.4589084 0.3490113 0.1920804
```

Confidence Intervals for Group Membership Probabilities

A narrow confidence interval of $\hat{\pi_k}$ implies that the probability is accurately estimated. These intervals are calculated by means of the bootstrap method.

```
R> ConfIntT(solL, Y = data[,2:11], A = data[,12:21], nb = 10000, alpha = 0.98)

         [,1]      [,2]      [,3]
1%  0.4399705 0.3332559 0.1828539
99% 0.4776469 0.3652074 0.2013546
```

Adequacy Matrix

trajeR allows to summarize these diagnostics in one table.

```
R> adequacy(solL,  Y = data[,2:11], A = data[,12:21], nb = 10000, alpha = 0.98)

                     1           2            3
Prob. est.   0.4589084   0.3490113 1.920804e-01
CI inf.      0.4400366   0.3333212 1.826260e-01
CI sup.      0.4770886   0.3650991 2.015266e-01
Prop.        0.4580000   0.3500000 1.920000e-01
AvePP        0.9957575   0.9918532 9.999998e-01
OCC        276.7406867 227.0867234 2.532774e+07
```

13 Conclusion