Package compilation for saemix 3.2 and basic run

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16/08/2022

Copy files

```r
cmd<-paste("rm -r ",file.path(workDir,"*"),sep="")
system(cmd)

dir.create(workDir)
```

```
## Warning in dir.create(workDir): '/home/eco/work/saemix/versions/saemix3.2'
## existe déjà
```

```r
dir.create(file.path(workDir,"saemix"))

cmd<-paste("cp -rp ",file.path(saemixDir,"documentation","docsaem.pdf")," ",file.path(saemixDir,"inst",
system(cmd)

cmd<-paste("cp -rp ",file.path(saemixDir,"R")," ", file.path(workDir,"saemix","/"),sep="")
system(cmd)
cmd<-paste("cp -rp ",file.path(saemixDir,"data")," ", file.path(workDir,"saemix","/"),sep="")
system(cmd)
cmd<-paste("cp -rp ",file.path(saemixDir,"inst")," ", file.path(workDir,"saemix","/"),sep="")
system(cmd)
for(ifile in c("CHANGES","DESCRIPTION")) {
  cmd<-paste("cp ",file.path(saemixDir,ifile)," ", file.path(workDir,"saemix"),sep="")
  system(cmd)
}
cmd<-paste("cp ",file.path(saemixDir,"inst","CITATION")," ", file.path(workDir,"saemix","inst"),sep="")
system(cmd)
```

Compilation

- building on win-ftp
    - to specify when submitting Possibly mis-spelled words in DESCRIPTION: IAME (17:930) al (17:663) et (17:660) github (17:954) saemix (17:965)
    - removed: Found the following (possibly) invalid URLs: URL: http://group.monolix.org/ From: DESCRIPTION Status: 403 Message: Forbidden
    - to change: no commas between keywords in R (maybe for vignettes)
    - previous version, solved now:

```r
Found the following \keyword or \concept entries
which likely give several index terms:
File 'backward.procedure.Rd':
  \keyword{backward,}
```

```
  \keyword{selection,}
... (others)
```
```

- Examples with CPU or elapsed time > 5s user system elapsed rapi.saemix 47.006 0.096 47.115 cow.saemix 25.185 0.120 25.311 PD1.saemix 18.925 0.048 19.108 toenail.saemix 16.656 0.020 16.676 compare.saemix 9.152 0.020 9.171 theo.saemix 6.481 0.008 6.490 yield.saemix 5.419 0.016 5.435

```r
setwd(workDir)
system("R CMD build saemix")

# Test examples
if(testExamples)
  system("R CMD check --as-cran --run-donttest saemix_3.2.tar.gz") else
    system("R CMD check --as-cran saemix_3.2.tar.gz")

# Reverse dependencies
cmd<-paste("cp ",file.path("/home/eco/work/saemix/versions/reverseDependencies/varTestnlme_1.3.0.tar.gz
system(cmd)

if(checkReverseDependencies) {
  # Check which packages depend on saemix
  package_dependencies(packages="saemix", reverse=TRUE)
  # TODO download these packages into workDir
}

if(installPackage) {
  # install saemix current version and check packages
  install.packages(pkgs=file.path(workDir,"saemix_3.2.tar.gz"),repos=NULL)
  #result <- check_packages_in_dir(workDir, revdep = list() )
  result <- check_packages_in_dir(workDir, revdep = list("varTestnlme") )
  summary(result)
}
```

Examples on CRAN   Examples with CPU or elapsed time > 5s user system elapsed rapi.saemix 32.510 0.092 32.602 cow.saemix 17.020 0.072 17.093 toenail.saemix 13.531 0.000 13.532 PD1.saemix 12.789 0.035 12.910 compare.saemix 6.331 0.016 6.347 theo.saemix 5.171 0.000 5.172

Warnings

Check

Install package in development mode

```r
dev_mode() # development mode
```

```
## v Dev mode: ON
```

```r
install.packages(pkgs=file.path(workDir,"saemix_3.2.tar.gz"),repos=NULL)
```

```
## Installation du package dans '/home/eco/R-dev'
## (car 'lib' n'est pas spécifié)
```

```r
library(saemix)
library(testthat)
```

```
##
```

```
## Attachement du package : 'testthat'
##
## L'objet suivant est masqué depuis 'package:devtools':
##
##     test_file
```

Running theopp example

```
?theo.saemix
```

```
## Aucune documentation pour 'theo.saemix' n'a été trouvée dans les packages et les bibliothèques :
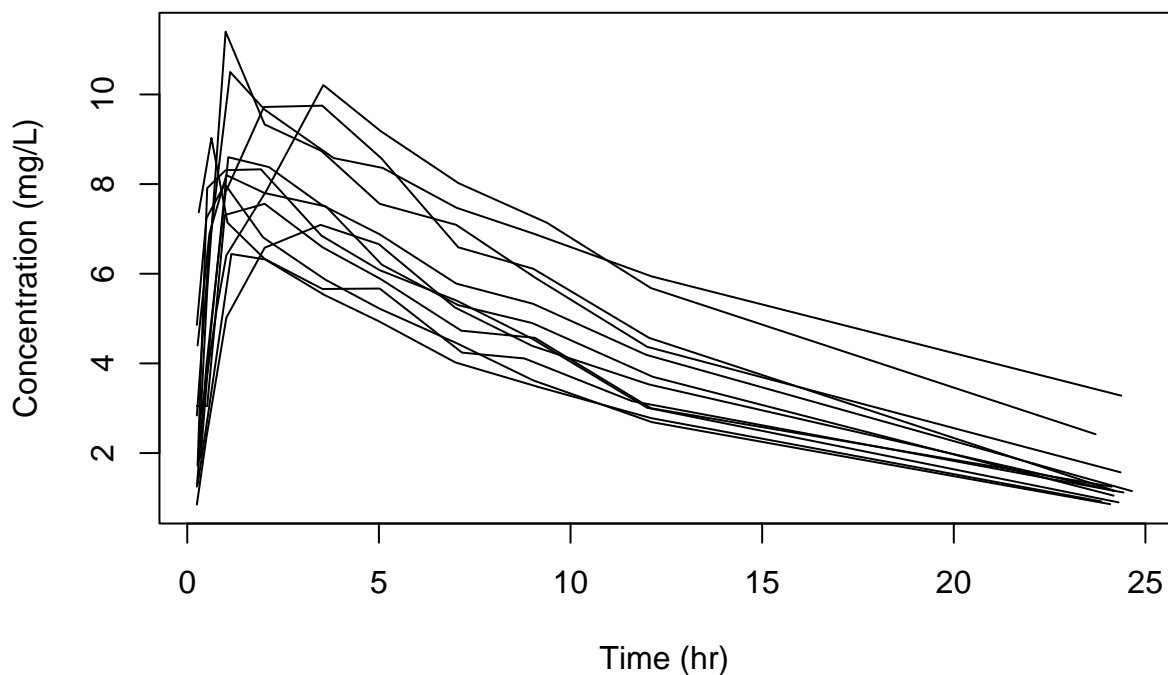## vous pourriez essayer '??theo.saemix'
```

```
?saemix
```

```
## Aucune documentation pour 'saemix' n'a été trouvée dans les packages et les bibliothèques :
## vous pourriez essayer '??saemix'
```

Run on the theophylline example

```
## Object of class SaemixData
##      longitudinal data for use with the SAEM algorithm
## Dataset theo.saemix
##      Structured data: Concentration ~ Dose + Time | Id
##      X variable for graphs: Time (hr)
##      covariates: Weight (kg), Sex (-)
##        reference class for covariate Sex :  0
## Dataset characteristics:
##      number of subjects:     12
##      number of observations: 120
##      average/min/max nb obs: 10.00  /  10  /  10
## First 10 lines of data:
##     Id    Dose   Time Concentration Weight Sex mdv cens occ ytype
## 1    1 319.992  0.25          2.84   79.6   1   0    0   1     1
## 2    1 319.992  0.57          6.57   79.6   1   0    0   1     1
## 3    1 319.992  1.12         10.50   79.6   1   0    0   1     1
## 4    1 319.992  2.02          9.66   79.6   1   0    0   1     1
## 5    1 319.992  3.82          8.58   79.6   1   0    0   1     1
## 6    1 319.992  5.10          8.36   79.6   1   0    0   1     1
## 7    1 319.992  7.03          7.47   79.6   1   0    0   1     1
## 8    1 319.992  9.05          6.89   79.6   1   0    0   1     1
## 9    1 319.992 12.12          5.94   79.6   1   0    0   1     1
## 10   1 319.992 24.37          3.28   79.6   1   0    0   1     1
```

```
## Nonlinear mixed-effects model
##   Model function:  One-compartment model with first-order absorption
##   Model type:  structural
## function(psi,id,xidep) {
##    dose<-xidep[,1]
##    tim<-xidep[,2]
##    ka<-psi[id,1]
##    V<-psi[id,2]
##    CL<-psi[id,3]
##    k<-CL/V
##    ypred<-dose*ka/(V*(ka-k))*(exp(-k*tim)-exp(-ka*tim))
##    return(ypred)
## }
##   Nb of parameters: 3
##       parameter names:  ka V CL
##        distribution:
##      Parameter Distribution Estimated
## [1,] ka         log-normal    Estimated
## [2,] V          log-normal    Estimated
## [3,] CL         log-normal    Estimated
##   Variance-covariance matrix:
##    ka V CL
## ka  1 0  0
## V   0 1  0
## CL  0 0  1
##   Error model: constant , initial values: a.1=1
##   Covariate model:
##      ka V CL
## [1,]  0 1  0
## [2,]  0 0  0
```

```
##      Initial values
##             ka  V    CL
## Pop.CondInit 1.0 20  0.50
## Cov.CondInit 0.1  0 -0.01

## Nonlinear mixed-effects model fit by the SAEM algorithm
## ----------------------------------
## ----            Data            ----
## ----------------------------------
## Object of class SaemixData
##      longitudinal data for use with the SAEM algorithm
## Dataset theo.saemix
##      Structured data: Concentration ~ Dose + Time | Id
##      X variable for graphs: Time (hr)
##      covariates: Weight (kg), Sex (-)
##       reference class for covariate Sex :  0
## Dataset characteristics:
##      number of subjects:      12
##      number of observations: 120
##      average/min/max nb obs: 10.00  /  10  /  10
## First 10 lines of data:
##     Id    Dose   Time Concentration Weight Sex mdv cens occ ytype
## 1    1 319.992  0.25          2.84   79.6   1   0    0   1     1
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## 3    1 319.992  1.12         10.50   79.6   1   0    0   1     1
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## 8    1 319.992  9.05          6.89   79.6   1   0    0   1     1
## 9    1 319.992 12.12          5.94   79.6   1   0    0   1     1
## 10   1 319.992 24.37          3.28   79.6   1   0    0   1     1
## ----------------------------------
## ----           Model           ----
## ----------------------------------
## Nonlinear mixed-effects model
##   Model function:  One-compartment model with first-order absorption
##   Model type:  structural
## function(psi,id,xidep) {
##     dose<-xidep[,1]
##     tim<-xidep[,2]
##     ka<-psi[id,1]
##     V<-psi[id,2]
##     CL<-psi[id,3]
##     k<-CL/V
##     ypred<-dose*ka/(V*(ka-k))*(exp(-k*tim)-exp(-ka*tim))
##     return(ypred)
## }
## <bytecode: 0x55fa8e987558>
##   Nb of parameters: 3
##       parameter names:  ka V CL
##       distribution:
##     Parameter Distribution Estimated
## [1,] ka         log-normal    Estimated
```

```
## [2,] V           log-normal    Estimated
## [3,] CL          log-normal    Estimated
##   Variance-covariance matrix:
##     ka V CL
## ka  1 0  0
## V   0 1  0
## CL  0 0  1
##   Error model: constant , initial values: a.1=1
##   Covariate model:
##        [,1] [,2] [,3]
## Weight    0   1    0
##     Initial values
##                ka  V    CL
## Pop.CondInit 1.0 20  0.50
## Cov.CondInit 0.1  0 -0.01
## --------------------------------
## ----    Key algorithm options  ----
## --------------------------------
##     Estimation of individual parameters (MAP)
##     Estimation of standard errors and linearised log-likelihood
##     Estimation of log-likelihood by importance sampling
##     Number of iterations:  K1=300, K2=100
##     Number of chains:  5
##     Seed:  632545
##     Number of MCMC iterations for IS:  5000
##     Simulations:
##         nb of simulated datasets used for npde:  1000
##         nb of simulated datasets used for VPC:  100
##     Input/output
##         save the results to a file:  FALSE
##         save the graphs to files:  FALSE
## ------------------------------------------------------
## ----                  Results                ----
## ------------------------------------------------------
## ----------------- Fixed effects  ------------------
## ------------------------------------------------------
##       Parameter        Estimate SE      CV(%) p-value
## [1,] ka                1.5588  0.3071 19.7  -
## [2,] V                18.8423  5.6328 29.9  -
## [3,] beta_Weight(V)    0.0073  0.0042 58.0  0.085
## [4,] CL                2.7717  0.2431  8.8  -
## [5,] a.1               0.7389  0.0565  7.7  -
## ------------------------------------------------------
## ----------- Variance of random effects  -----------
## ------------------------------------------------------
##    Parameter Estimate SE     CV(%)
## ka omega2.ka 0.414    0.1853 45
## V  omega2.V  0.012    0.0078 64
## CL omega2.CL 0.077    0.0368 48
## ------------------------------------------------------
## ------ Correlation matrix of random effects  ------
## ------------------------------------------------------
##           omega2.ka omega2.V omega2.CL
## omega2.ka 1         0        0
```

```
## omega2.V   0          1          0
## omega2.CL  0          0          1
## ----------------------------------------------------------
## ---------------  Statistical criteria  -------------
## ----------------------------------------------------------
## Likelihood computed by linearisation
##         -2LL= 341.3649
##         AIC = 357.3649
##         BIC = 361.2442
##
## Likelihood computed by importance sampling
##         -2LL= 342.6478
##         AIC = 358.6478
##         BIC = 362.5271
## ----------------------------------------------------------
##
## Nonlinear mixed-effects model fit by the SAEM algorithm
## ----------------------------------
## ----           Data            ----
## ----------------------------------
## Object of class SaemixData
##      longitudinal data for use with the SAEM algorithm
## Dataset theo.saemix
##      Structured data: Concentration ~ Dose + Time | Id
##      X variable for graphs: Time (hr)
##      covariates: Weight (kg), Sex (-)
##        reference class for covariate Sex :  0
## Dataset characteristics:
##      number of subjects:     12
##      number of observations: 120
##      average/min/max nb obs: 10.00  /  10  /  10
## First 10 lines of data:
##     Id    Dose   Time Concentration Weight Sex mdv cens occ ytype
## 1    1 319.992  0.25          2.84   79.6   1   0    0   1     1
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## 3    1 319.992  1.12         10.50   79.6   1   0    0   1     1
## 4    1 319.992  2.02          9.66   79.6   1   0    0   1     1
## 5    1 319.992  3.82          8.58   79.6   1   0    0   1     1
## 6    1 319.992  5.10          8.36   79.6   1   0    0   1     1
## 7    1 319.992  7.03          7.47   79.6   1   0    0   1     1
## 8    1 319.992  9.05          6.89   79.6   1   0    0   1     1
## 9    1 319.992 12.12          5.94   79.6   1   0    0   1     1
## 10   1 319.992 24.37          3.28   79.6   1   0    0   1     1
## ----------------------------------
## ----          Model            ----
## ----------------------------------
## Nonlinear mixed-effects model
##   Model function:  One-compartment model with first-order absorption
##   Model type:  structural
## function(psi,id,xidep) {
##     dose<-xidep[,1]
##     tim<-xidep[,2]
##     ka<-psi[id,1]
##     V<-psi[id,2]
```

```
##     CL<-psi[id,3]
##     k<-CL/V
##     ypred<-dose*ka/(V*(ka-k))*(exp(-k*tim)-exp(-ka*tim))
##     return(ypred)
## }
## <bytecode: 0x55fa8e987558>
##   Nb of parameters: 3
##       parameter names:  ka V CL
##       distribution:
##       Parameter Distribution Estimated
## [1,] ka          log-normal   Estimated
## [2,] V           log-normal   Estimated
## [3,] CL          log-normal   Estimated
##   Variance-covariance matrix:
##    ka V CL
## ka  1 0  0
## V   0 1  0
## CL  0 0  1
##   Error model: constant , initial values: a.1=1
##   Covariate model:
##       [,1] [,2] [,3]
## Weight    0    1    0
##     Initial values
##              ka   V    CL
## Pop.CondInit 1.0 20  0.50
## Cov.CondInit 0.1  0 -0.01
## -------------------------------------
## ----      Key algorithm options  ----
## -------------------------------------
##     Estimation of individual parameters (MAP)
##     Estimation of standard errors and linearised log-likelihood
##     Estimation of log-likelihood by importance sampling
##     Number of iterations: K1=300, K2=100
##     Number of chains:  5
##     Seed:  632545
##     Number of MCMC iterations for IS:  5000
##     Simulations:
##         nb of simulated datasets used for npde:  1000
##         nb of simulated datasets used for VPC:  100
##     Input/output
##         save the results to a file:  FALSE
##         save the graphs to files:  FALSE
## ------------------------------------------------------
## ----                    Results                   ----
## ------------------------------------------------------
## ----------------- Fixed effects  ------------------
## ------------------------------------------------------

## Warning in .local(x, ...): NAs introduits lors de la conversion automatique

##      Parameter       Estimate SE      CV(%) p-value
## [1,] ka               1.5588  0.3071 19.7  -
## [2,] V               18.8423  5.6328 29.9  -
## [3,] beta_Weight(V)   0.0073  0.0042 58.0  0.085
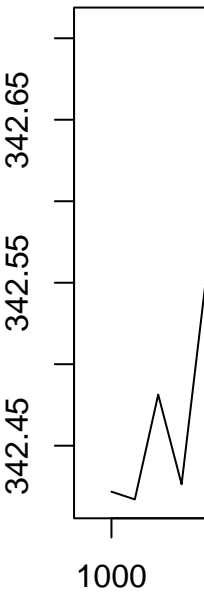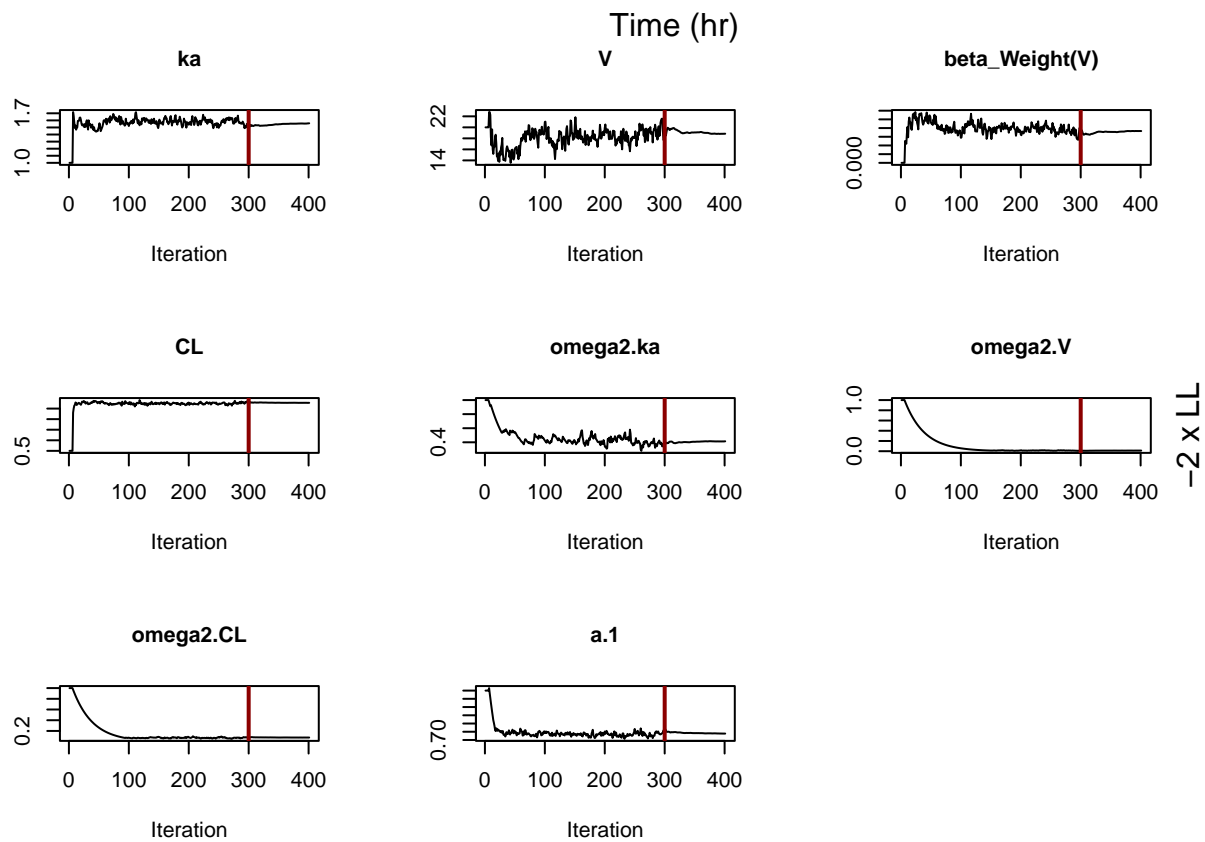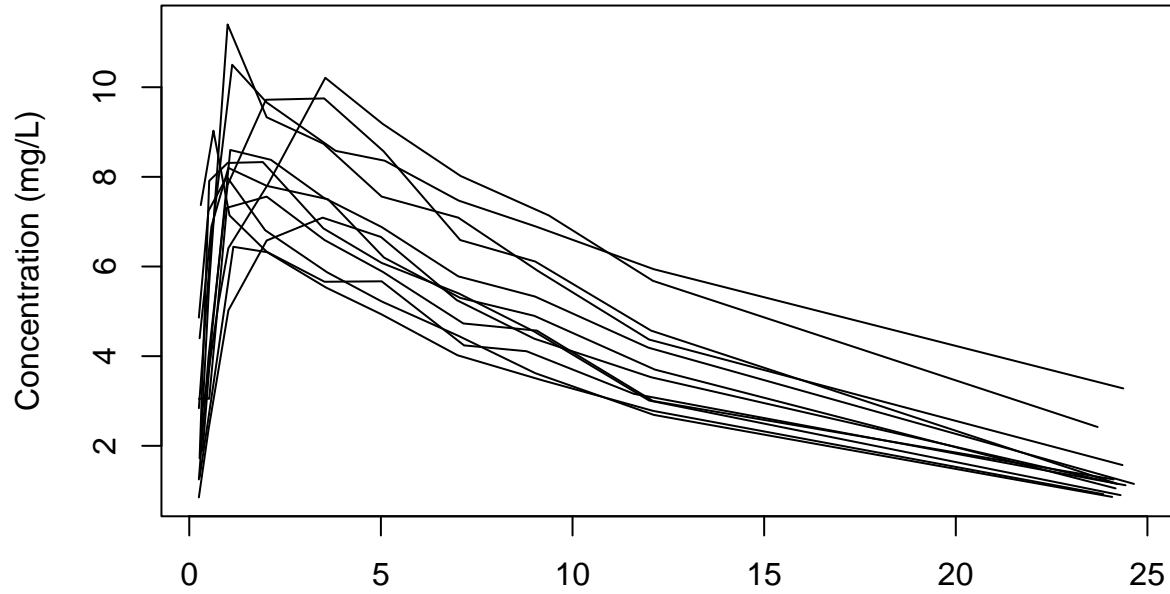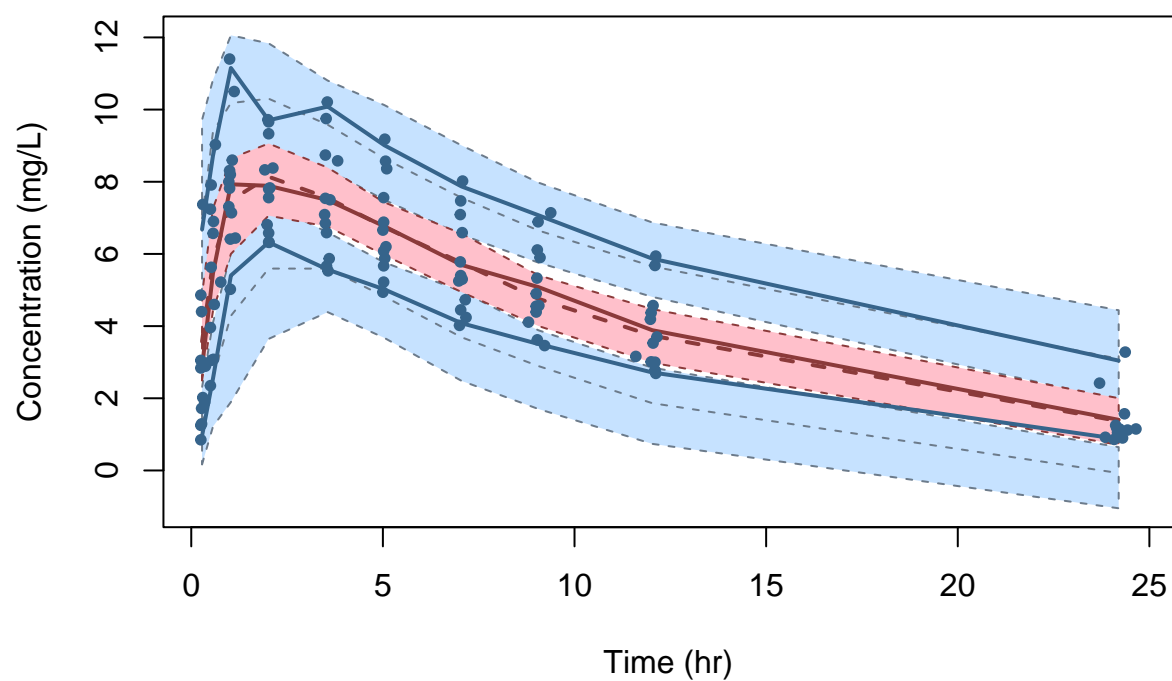## [4,] CL               2.7717  0.2431  8.8  -
```

```
## [5,] a.1                0.7389  0.0565  7.7  -
## -------------------------------------------------------
## -----------  Variance of random effects  -----------
## -------------------------------------------------------
##     Parameter Estimate SE    CV(%)
## ka omega2.ka 0.414     0.1853 45
## V  omega2.V  0.012     0.0078 64
## CL omega2.CL 0.077     0.0368 48
## -------------------------------------------------------
## ------  Correlation matrix of random effects  ------
## -------------------------------------------------------
##           omega2.ka omega2.V omega2.CL
## omega2.ka 1          0        0
## omega2.V  0          1        0
## omega2.CL 0          0        1
## -------------------------------------------------------
## ---------------  Statistical criteria  -------------
## -------------------------------------------------------
## Likelihood computed by linearisation
##       -2LL= 341.3649
##       AIC = 357.3649
##       BIC = 361.2442
##
## Likelihood computed by importance sampling
##       -2LL= 342.6478
##       AIC = 358.6478
##       BIC = 362.5271
## -------------------------------------------------------

## Object of class SaemixSimData
##     data simulated according to a non-linear mixed effect model
## Characteristics of original data
##     number of subjects: 12
##     summary of response:
##   Min. 1st Qu.  Median   Mean 3rd Qu.    Max.
##   0.850   3.513   5.665   5.447   7.325  11.400
## Characteristics of simulated data
##     number of simulated datasets: 1000
##     summary of simulated response
##   Min. 1st Qu.  Median   Mean 3rd Qu.    Max.
##  -2.364   3.675   5.615   5.479   7.359  14.679

##          ka        V       CL
## 1  1.7863333 29.59934 1.681678
## 2  1.9372081 31.98292 3.178891
## 3  2.2543380 33.18598 2.854727
## 4  1.2081689 31.53805 2.694492
## 5  1.4877219 27.10964 2.399152
## 6  1.0608154 38.09466 4.028817
## 7  0.6907825 32.17493 3.280839
## 8  1.3001684 34.17845 3.297077
## 9  6.3284102 32.50705 2.832542
## 10 0.7559841 26.58247 1.891913
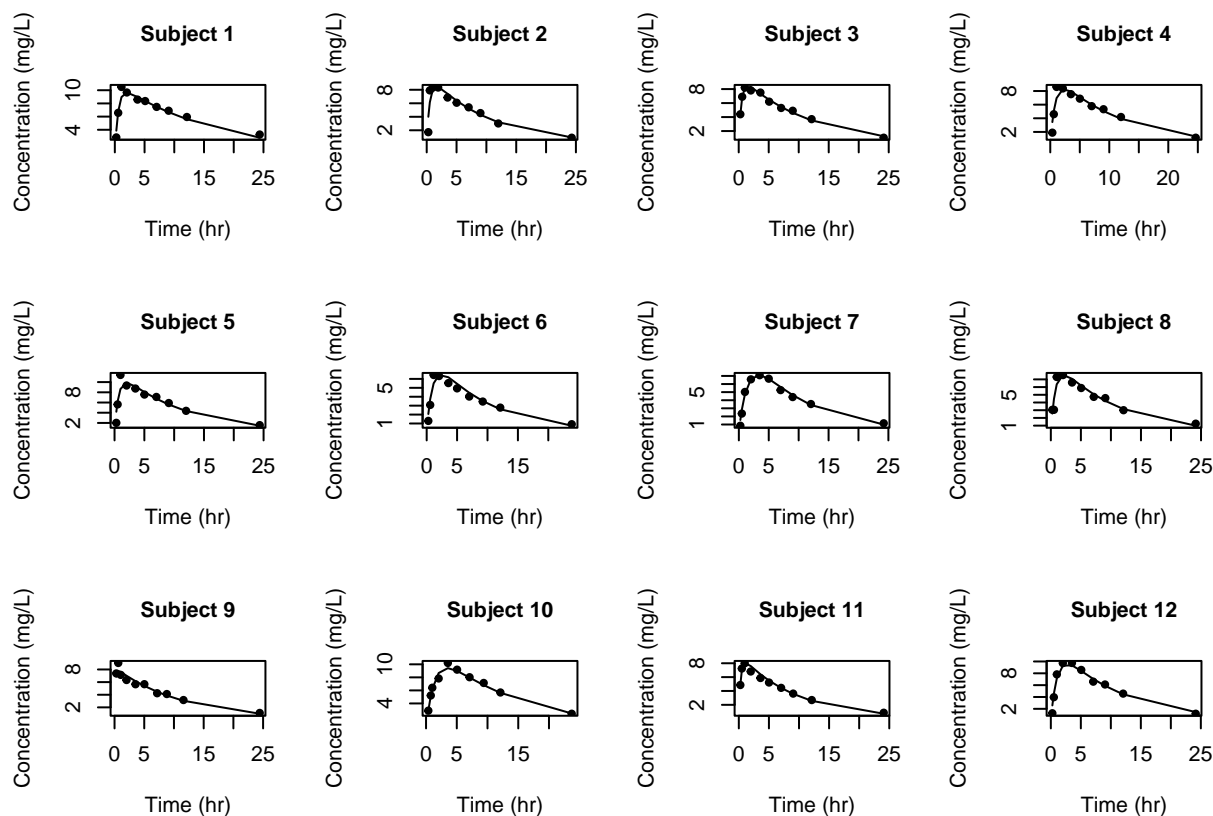## 11 3.1478359 35.17647 3.763632
## 12 0.9503826 26.06740 2.424328
```

Plot results:

```
## Simulating data using nsim = 1000 simulated datasets
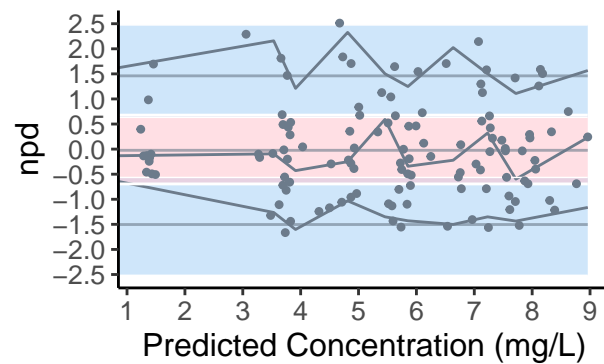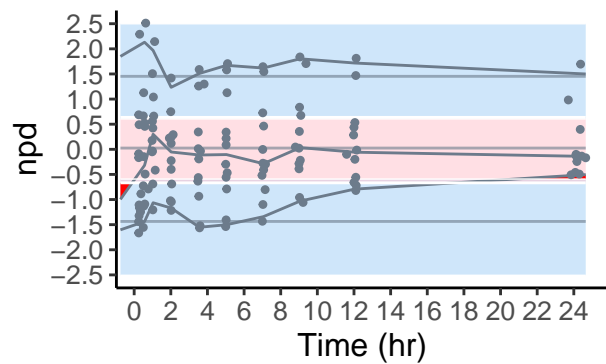## Computing WRES and npde ..
```

Population predictions

Individual predictions, MAP

Visual Predictive Check


```
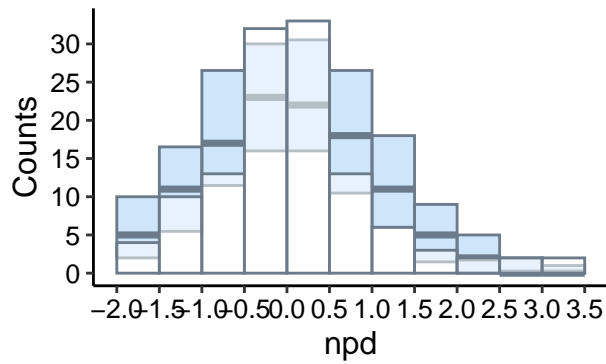## Computing WRES and npde ..
```

Subject 1 Concentration (mg/L) Time (hr)
Subject 2 Concentration (mg/L) Time (hr)
Subject 3 Concentration (mg/L) Time (hr)
Subject 4 Concentration (mg/L) Time (hr)
Subject 5 Concentration (mg/L) Time (hr)
Subject 6 Concentration (mg/L) Time (hr)
Subject 7 Concentration (mg/L) Time (hr)
Subject 8 Concentration (mg/L) Time (hr)
Subject 9 Concentration (mg/L) Time (hr)
Subject 10 Concentration (mg/L) Time (hr)
Subject 11 Concentration (mg/L) Time (hr)
Subject 12 Concentration (mg/L) Time (hr)

```
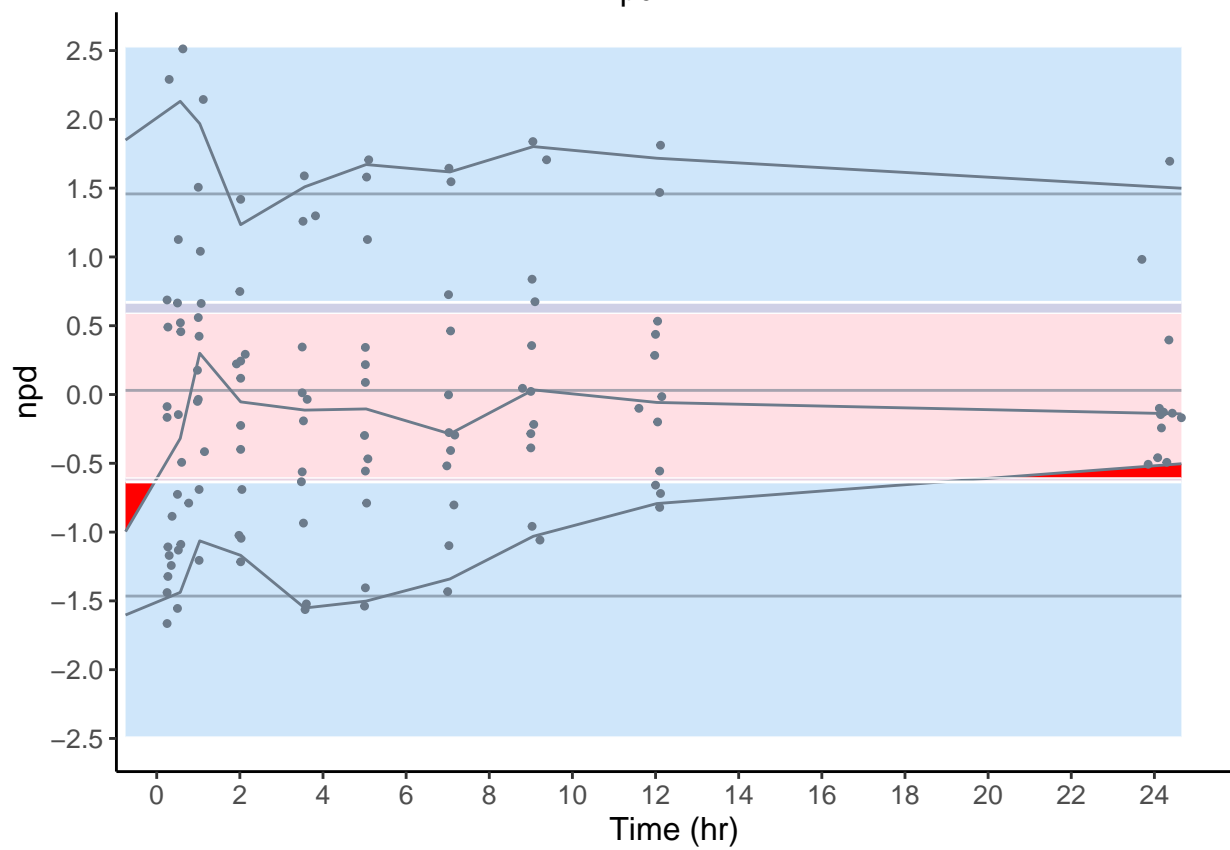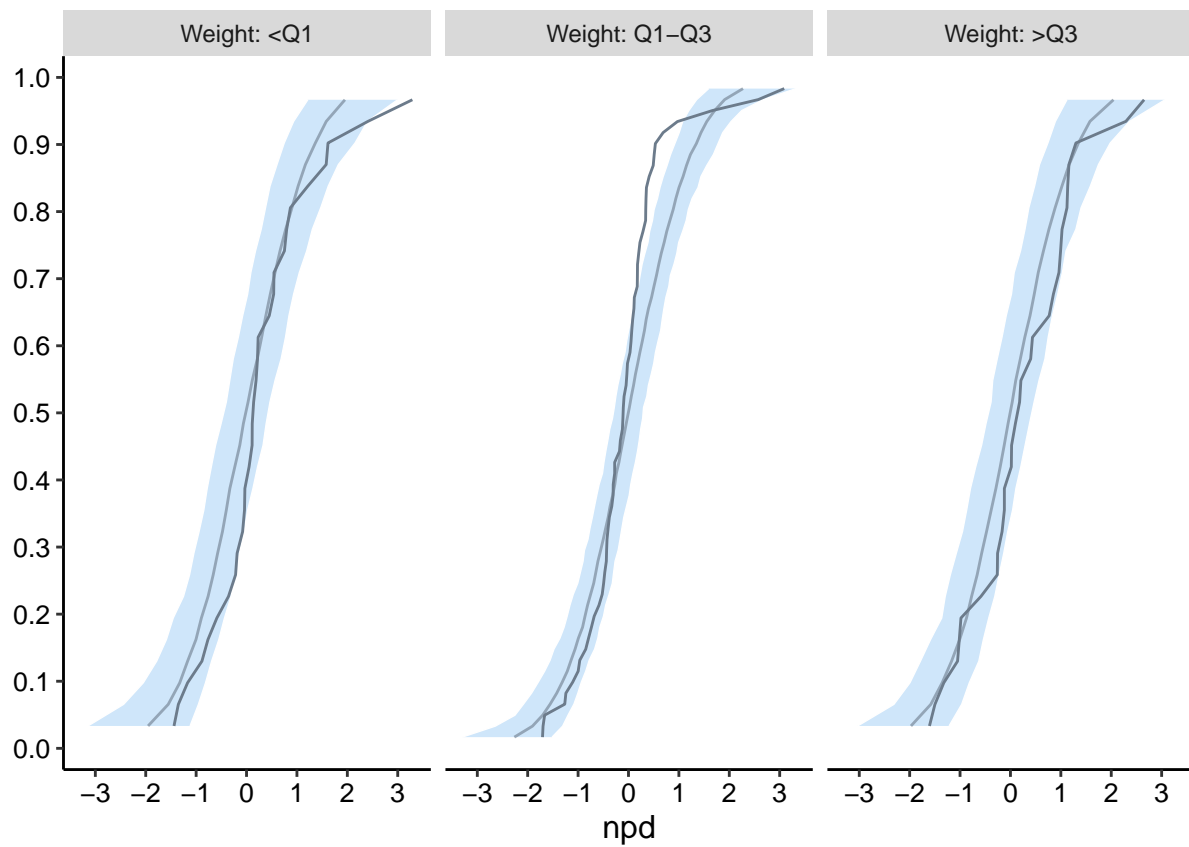## Computing WRES and npde ..

## Please use npdeSaemix to obtain VPC and npde

## Warning in read(x, dat, detect = detect, verbose = verbose): NAs introduits lors
## de la conversion automatique

## Warning in read(x, dat, detect = detect, verbose = verbose): NAs introduits lors
## de la conversion automatique

## Warning in read(x, dat, detect = detect, verbose = verbose): NAs introduits lors
## de la conversion automatique

## Warning in read(x, dat, detect = detect, verbose = verbose): NAs introduits lors
## de la conversion automatique

## Warning in read(x, dat, detect = detect, verbose = verbose): NAs introduits lors
## de la conversion automatique

## Warning in which(!is.na(as.integer(object@name.covariates))): NAs introduits
## lors de la conversion automatique

## -----------------------------------------------
## Distribution of npde :
##        nb of obs: 120
##              mean= 0.07039    (SE= 0.087 )
##          variance= 0.9023    (SE= 0.12 )
##          skewness= 0.8593
##          kurtosis= 1.542
## -----------------------------------------------
```

```
## Statistical tests (adjusted p-values):
##    t-test                : 1
##    Fisher variance test  : 1
##    SW test of normality  : 0.000231 ***
##    Global test           : 0.000231 ***
## ---
## Signif. codes: '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1
## -------------------------------------------
```

v Dev mode: OFF