

# Package compilation for saemix 3.2 and basic run

Emmanuelle Comets

16/08/2022

## Copy files

```
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

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

```
# Reduce size of viral load simulation data (to 500 simulations) for CRAN
knitr::opts_chunk$set(root.dir = file.path(workDir, "saemix"))
setwd(file.path(workDir, "saemix"))

devtools::document(file.path(workDir, "saemix"))
```

```
## i Updating saemix documentation
## First time using roxygen2. Upgrading automatically...
## i Loading saemix
## Loading required package: npde
## Package saemix, version 3.2
## please direct bugs, questions and feedback to emmanuelle.comets@inserm.fr

## Writing NAMESPACE
## Writing NAMESPACE
## Writing readSaemix-methods.Rd
## Writing showall-methods.Rd
## Writing psi-methods.Rd
## Writing initialize-methods.Rd
## Writing print-methods.Rd
## Writing show-methods.Rd
## Writing summary-methods.Rd
## Writing predict-methods.Rd
## Writing plot-methods.Rd
## Writing saemix.internal.Rd
## Writing theo.saemix.Rd
## Writing PD1.saemix.Rd
## Writing oxboys.saemix.Rd
## Writing cow.saemix.Rd
## Writing yield.saemix.Rd
## Writing toenail.saemix.Rd
## Writing knee.saemix.Rd
## Writing lung.saemix.Rd
## Writing epilepsy.saemix.Rd
## Writing rapi.saemix.Rd
## Writing SaemixData-class.Rd
## Writing extract-methods.Rd
## Writing validate.names.Rd
## Writing read-methods.Rd
## Writing plot-SaemixData.Rd
## Writing saemixData.Rd
## Writing transform.Rd
## Writing transformContCov.Rd
## Writing transformCatCov.Rd
## Writing subset.Rd
## Writing SaemixModel-class.Rd
```

```

## Writing sub-SaemixModel-method.Rd
## Writing plot-SaemixModel.Rd
## Writing predict.SaemixModel.Rd
## Writing plot-SaemixModel-SaemixData-method.Rd
## Writing saemixModel.Rd
## Writing mydiag.Rd
## Writing validate.covariance.model.Rd
## Writing SaemixRes-class.Rd
## Writing sub-SaemixRes-method.Rd
## Writing resid.saemix.Rd
## Writing fitted.saemix.Rd
## Writing vcov.Rd
## Writing SaemixObject-class.Rd
## Writing saemixControl.Rd
## Writing sub-SaemixObject-method.Rd
## Writing saemix.predict.Rd
## Writing plot-SaemixObject-ANY-method.Rd
## Writing logLik.Rd
## Writing coef.saemix.Rd
## Writing replaceData.Rd
## Writing createSaemixObject.Rd
## Writing backward.procedure.Rd
## Writing llis.saemix.Rd
## Writing llgq.saemix.Rd
## Writing forward.procedure.Rd
## Writing fim.saemix.Rd
## Writing map.saemix.Rd
## Writing testnpde.Rd
## Writing compare.saemix.Rd
## Writing conddist.saemix.Rd
## Writing saemixPredictNewdata.Rd
## Writing npdeSaemix.Rd
## Writing saemix.plot.setoptions.Rd
## Writing saemix.plot.select.Rd
## Writing default.saemix.plots.Rd
## Writing saemix.plot.data.Rd
## Writing simulate.SaemixObject.Rd
## Writing simulateDiscreteSaemix.Rd
## Writing step.saemix.Rd
## Writing saemix.Rd
## Writing stepwise.procedure.Rd

```

```
roxygenise()
```

```

## i Loading saemix

## Package saemix, version 3.2
##   please direct bugs, questions and feedback to emmanuelle.comets@inserm.fr

## Writing NAMESPACE
## Writing NAMESPACE

```

```

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

```

dev_mode() # development mode

## v Dev mode: ON

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

## Installing package into '/home/eco/R-dev'
## (as 'lib' is unspecified)

library(saemix)
library(testthat)

##
## Attaching package: 'testthat'

## The following object is masked from 'package:devtools':
##
##   test_file

```

### Running theopp example

Documentation not found

```
?theo.saemix
```

```
## No documentation for 'theo.saemix' in specified packages and libraries:
## you could try '??theo.saemix'
```

```
?saemix
```

```
## No documentation for 'saemix' in specified packages and libraries:
## you could try '??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
## 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
## -----
## 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: 0x55e4165f7488>
##   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  0.042
## [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
## 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
## -----
## ----- 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: 0x55e4165f7488>
## 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 0.042
## [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
## -----
##      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
##
## Object of class SaemixSimData
##      data simulated according to a non-linear mixed effect model
##
## Object of class SaemixSimData

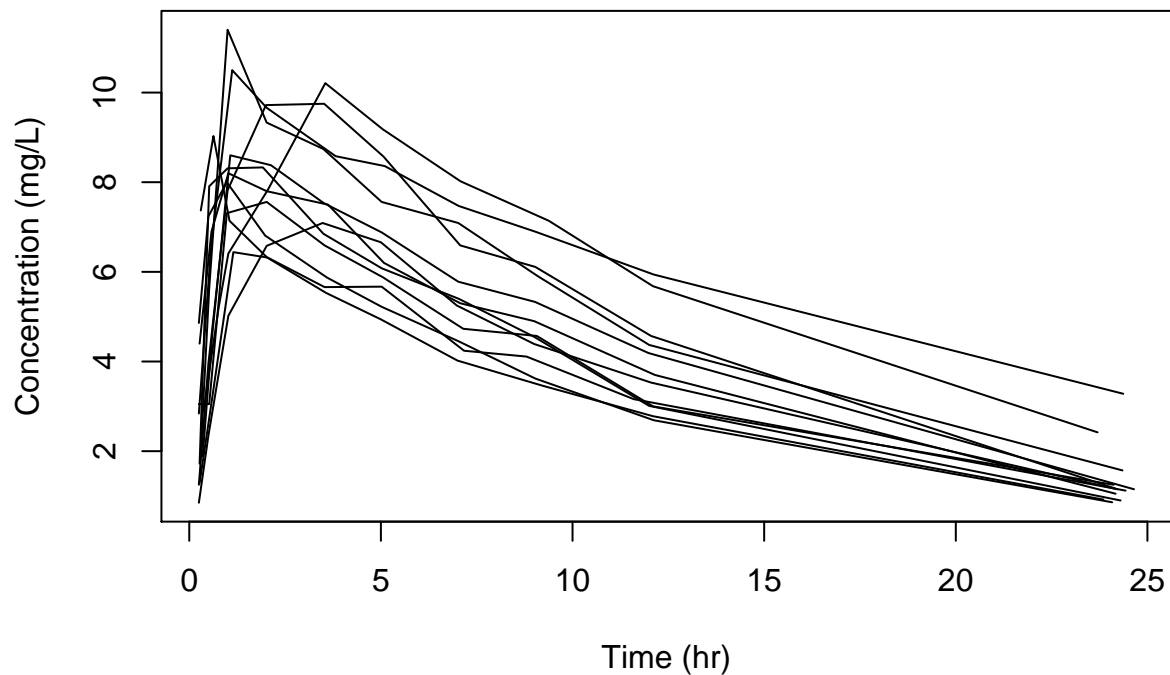
```

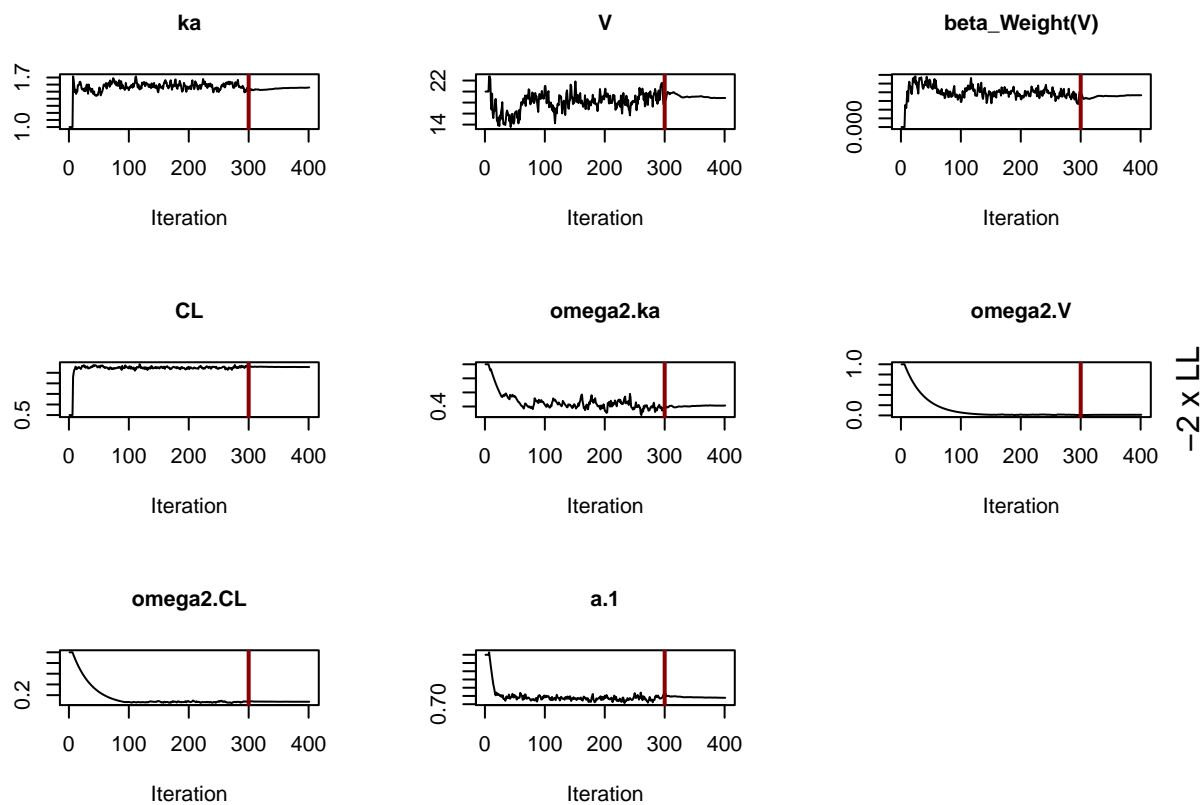
```
##      data simulated according to a non-linear mixed effect model
## Characteristics of original data
##      number of subjects: 12
##      summary of response:
##      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##      0.850  3.513  5.665  5.447  7.325  11.400
## Characteristics of simulated 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

## 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

## [1] TRUE
```

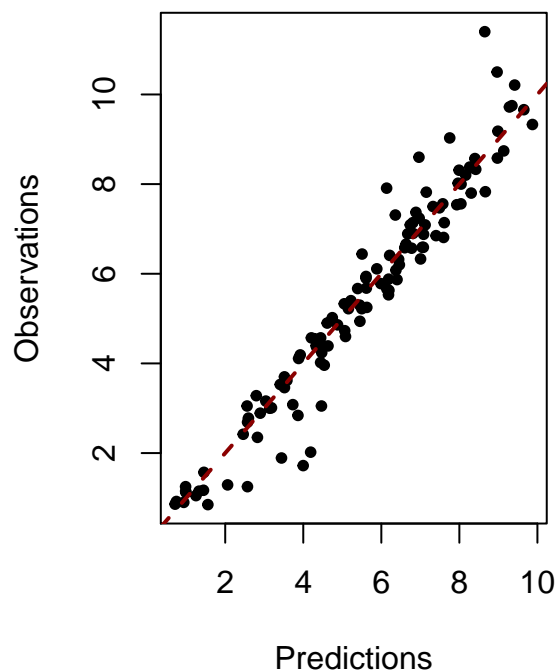
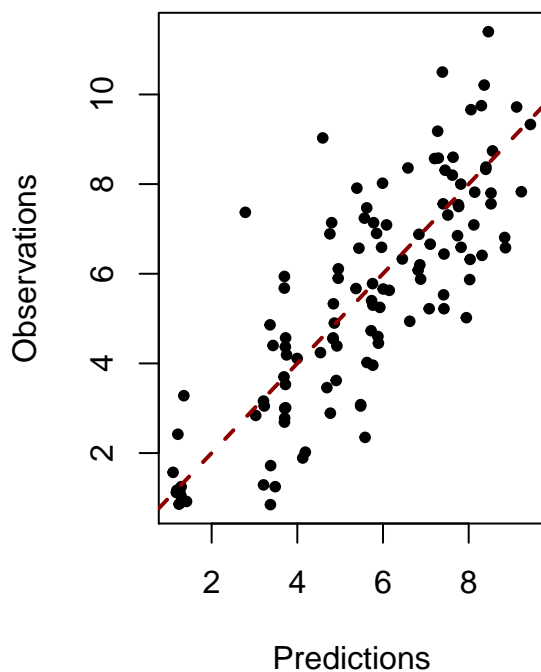
Plot results:



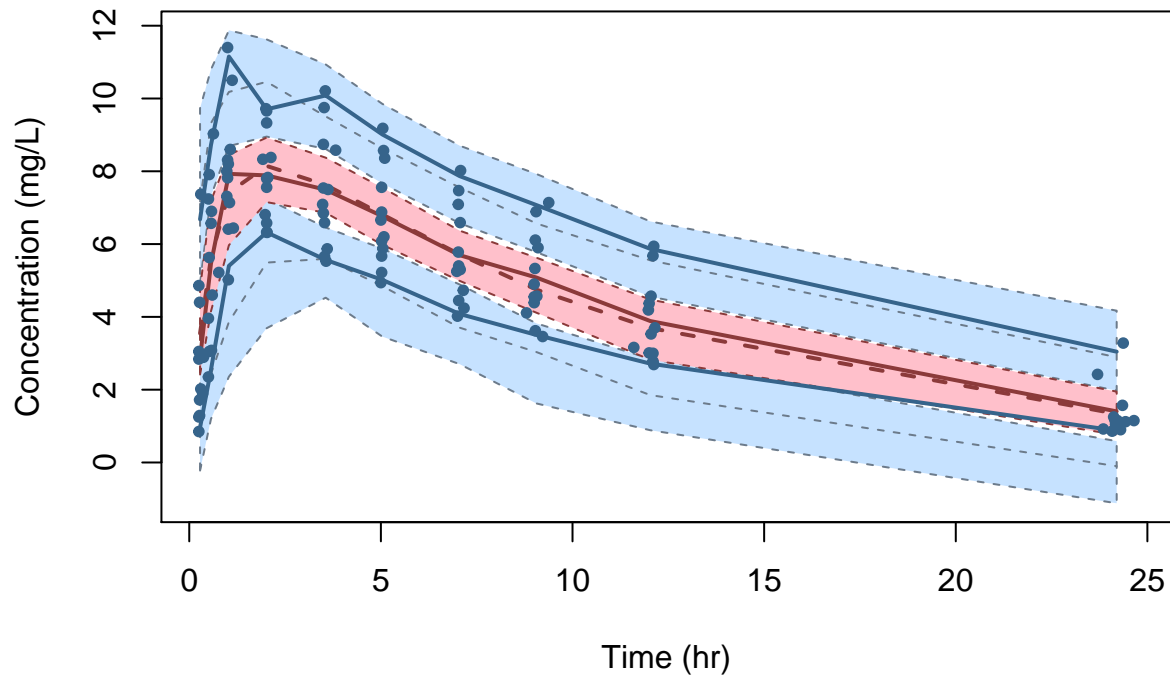


**Population predictions**

**Individual predictions, MAP**



## Visual Predictive Check



```
## 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

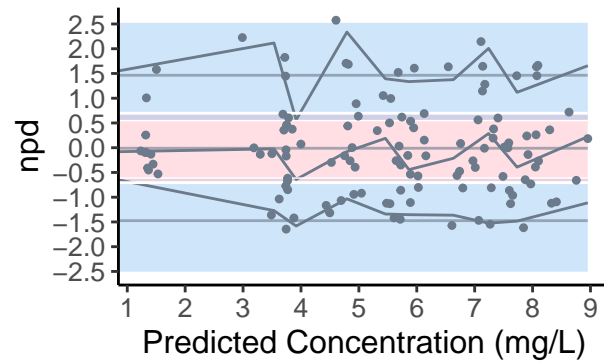
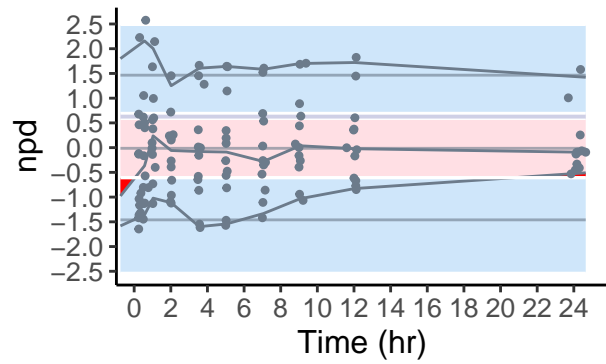
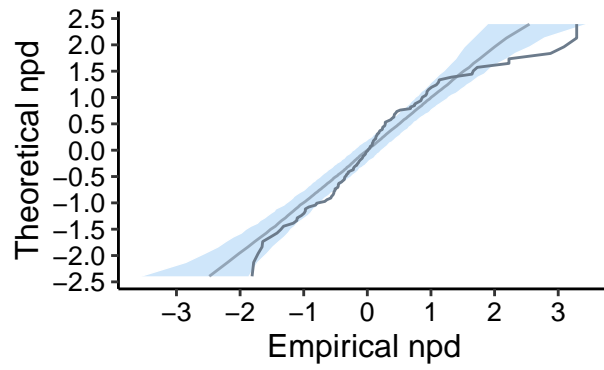
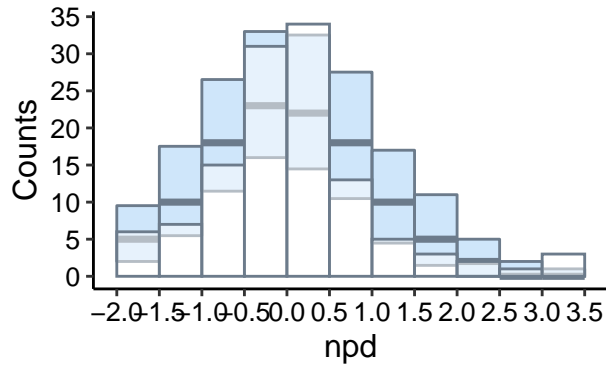
## Warning in read(x, dat, detect = detect, verbose = verbose): NAs introduits lors
## de la conversion automatique

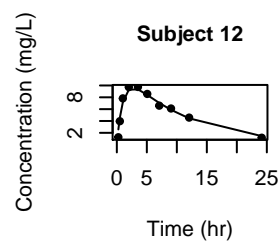
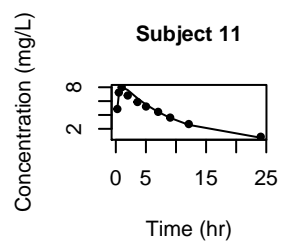
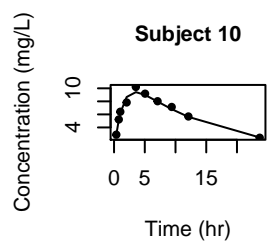
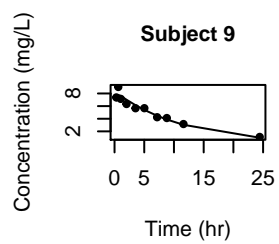
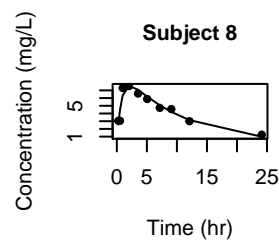
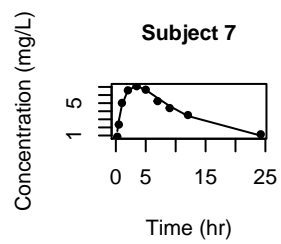
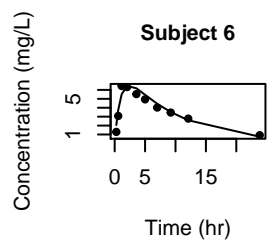
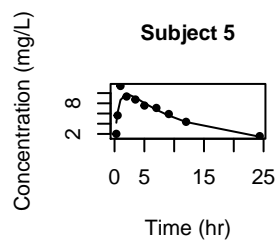
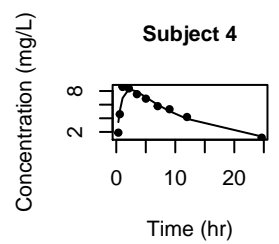
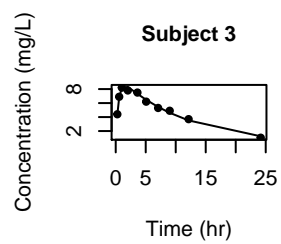
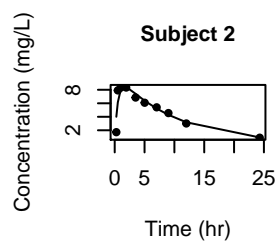
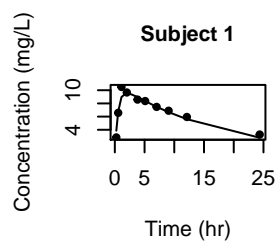
## Warning in read(x, dat, detect = detect, verbose = verbose): NAs introduits lors
## de la conversion automatique

## 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= 0.07365   (SE= 0.089 )
##      variance= 0.9433   (SE= 0.12 )
##      skewness= 0.9405
##      kurtosis= 1.958
## -----
## Statistical tests (adjusted p-values):
```

```
## t-test : 1
## Fisher variance test : 1
## SW test of normality : 3.94e-05 ***
## Global test : 3.94e-05 ***
## ---
## Signif. codes: '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1
## -----
```





## v Dev mode: OFF