Package compilation for saemix 3.0 and basic run

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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/saemix3.0'
## existe déjà
```

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

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

```
# 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...
## Updating collate directive in  /home/eco/work/saemix/versions/saemix3.0/saemix/DESCRIPTION
## i Loading saemix
## Loading required package: npde
```

```
## Package saemix, version 3.0
##   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 3.0
##   please direct bugs, questions and feedback to emmanuelle.comets@inserm.fr
```

```
## Writing NAMESPACE
## Writing NAMESPACE
```

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



testExamples<-TRUE
# Test examples
if(testExamples) system("R CMD check --as-cran --run-donttest saemix_3.0.tar.gz") else system("R CMD ch
```

Examples on CRAN

Examples with CPU or elapsed time > 5s user system elapsed rapi.saemix 37.043 0.148 37.203 cow.saemix 17.601 0.096 17.698 toenail.saemix 13.748 0.020 13.769 PD1.saemix 12.040 0.040 12.083 compare.saemix 6.702 0.012 6.716 theo.saemix 5.675 0.040 5.715 yield.saemix 4.980 0.041 5.021

Warnings

Check

Install package in development mode

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

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

```
install.packages(pkgs=file.path(workDir,"saemix_3.0.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
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## 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: 0x558525302598>
##   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 (-)
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## Dataset characteristics:
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##     number of observations: 120
##     average/min/max nb obs: 10.00  /  10  /  10
## First 10 lines of data:
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## 4   1 319.992  2.02          9.66   79.6   1   0    0   1     1
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## 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
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##    CL<-psi[id,3]
##    k<-CL/V
##    ypred<-dose*ka/(V*(ka-k))*(exp(-k*tim)-exp(-ka*tim))
##    return(ypred)
## }
## <bytecode: 0x558525302598>
##   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
```
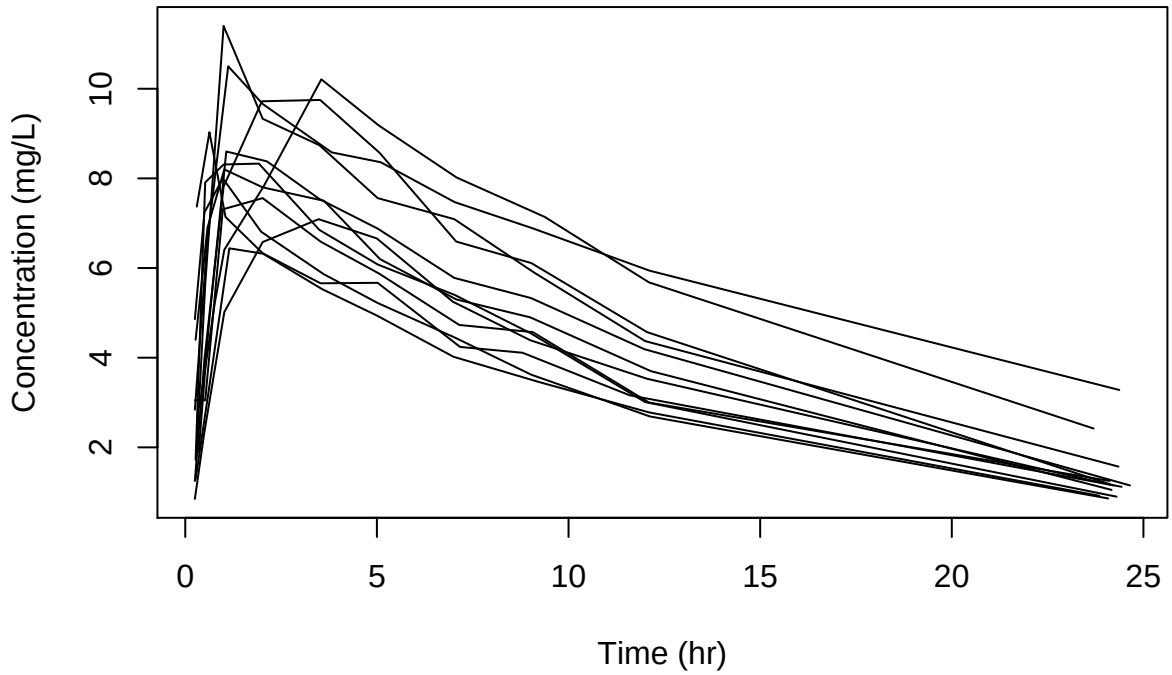
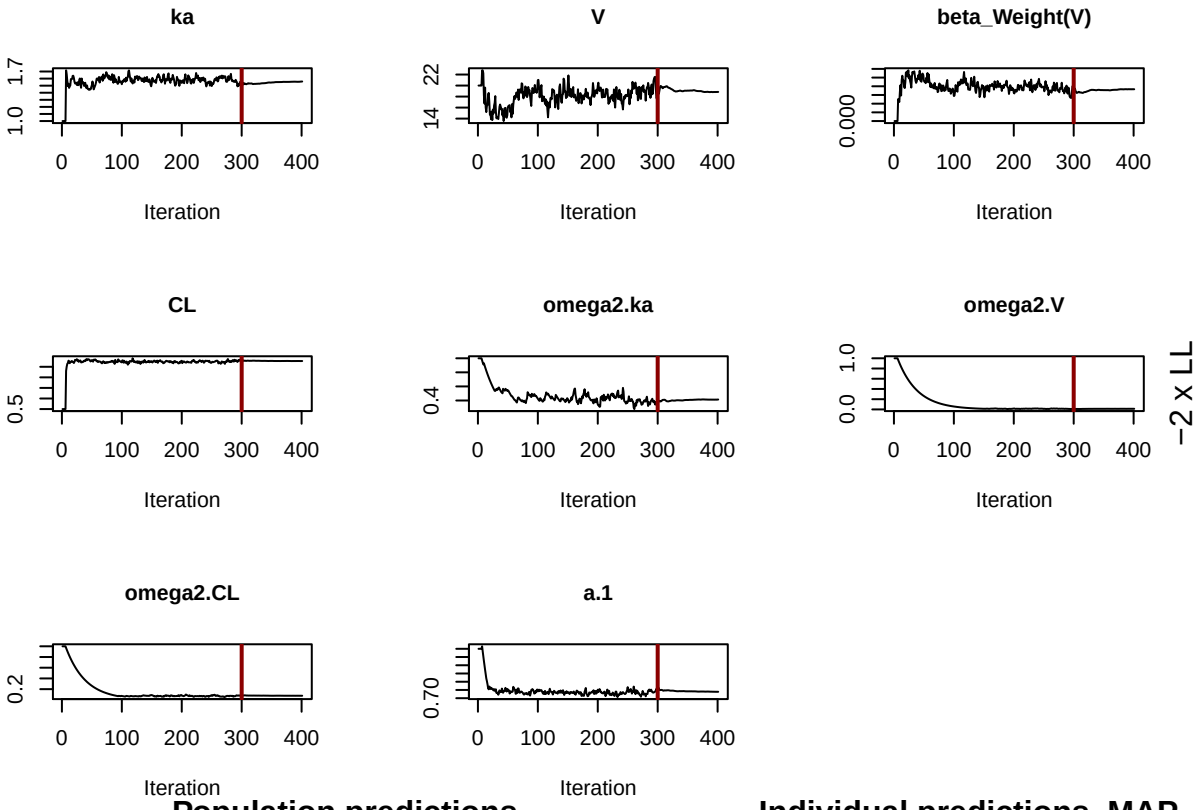

```
##   Error model: constant , initial values: a.1=1
##   Covariate model:
##        [,1] [,2] [,3]
## Weight    0    1    0
##     Initial values
##               ka  V    CL
## Pop.CondInit 1.0 20  0.50
## Cov.CondInit 0.1  0 -0.01
## ----------------------------------
## ----    Key algorithm options  ----
## ----------------------------------
##     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  -------------
## ----------------------------------------------------
```

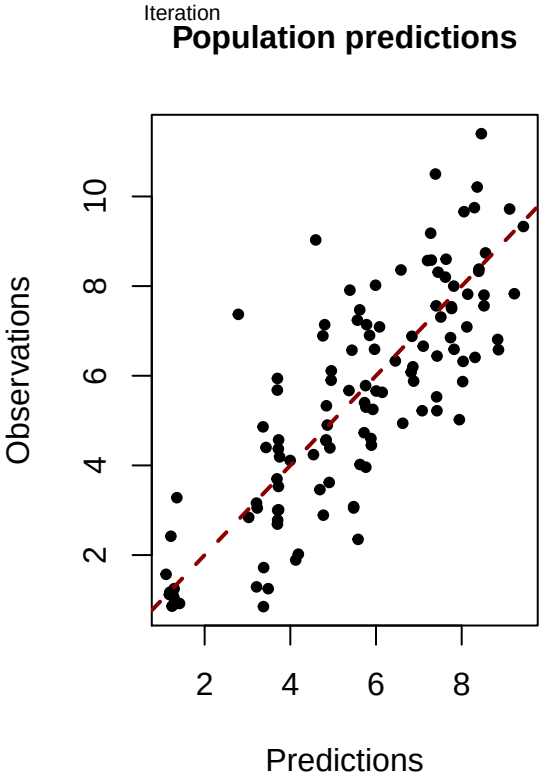
```
## Likelihood computed by linearisation
##       -2LL= 341.3649
##       AIC = 357.3649
##       BIC = 361.2442
##
## Likelihood computed by importance sampling
##       -2LL= 342.6478
##       AIC = 358.6478
##       BIC = 362.5271
## ----------------------------------------------------
```

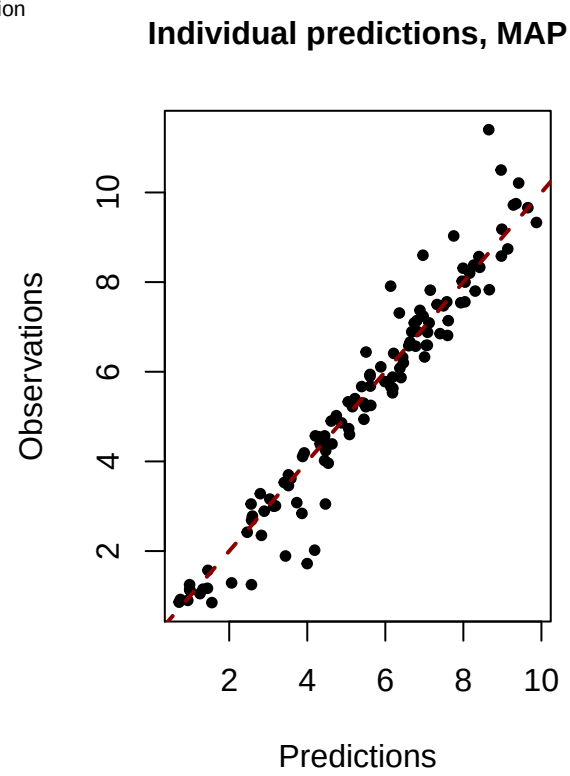
```
##           ka        V       CL
## 1  1.7863333 29.59934 1.681678
## 2  1.9372081 31.98292 3.178891
## 3  2.2543380 33.18598 2.854727
## 4  1.2081689 31.53805 2.694492
## 5  1.4877219 27.10964 2.399152
## 6  1.0608154 38.09466 4.028817
## 7  0.6907825 32.17493 3.280839
## 8  1.3001684 34.17845 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
```

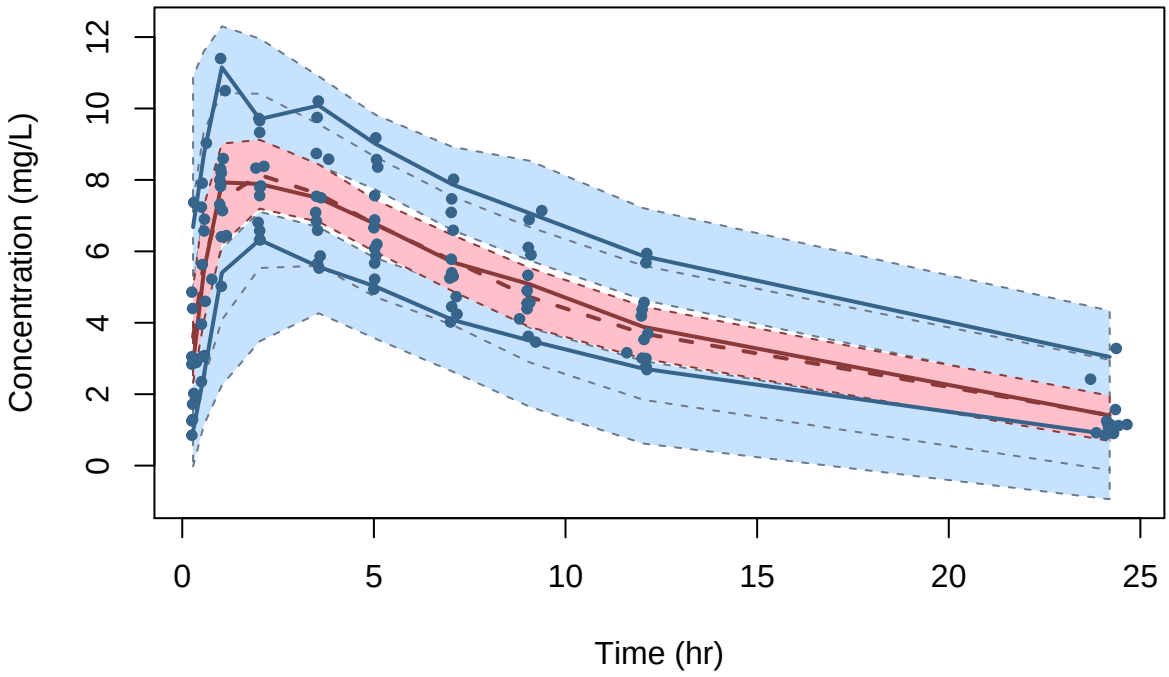
Plot results:




ka
V
beta_Weight(V)
CL
omega2.ka
omega2.V
omega2.CL
a.1
Iteration
−2 x LL
342.65
342.55
342.45
1000

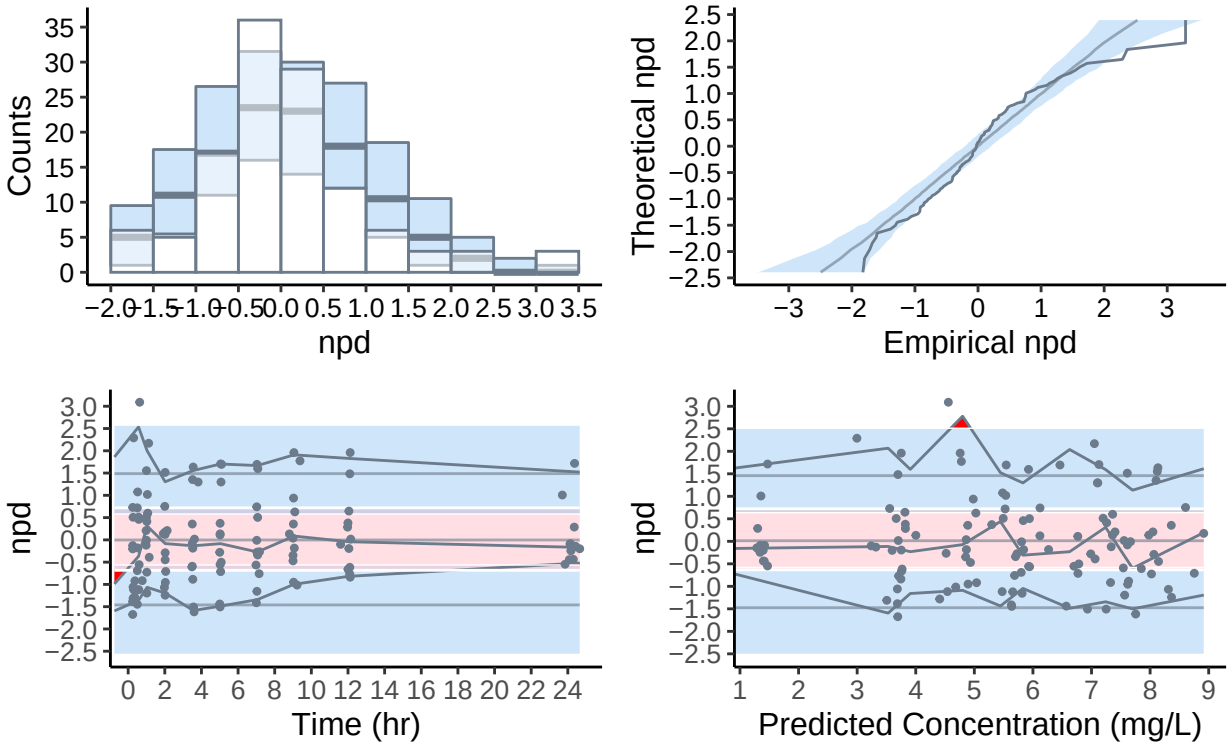

Population predictions
Observations
Predictions

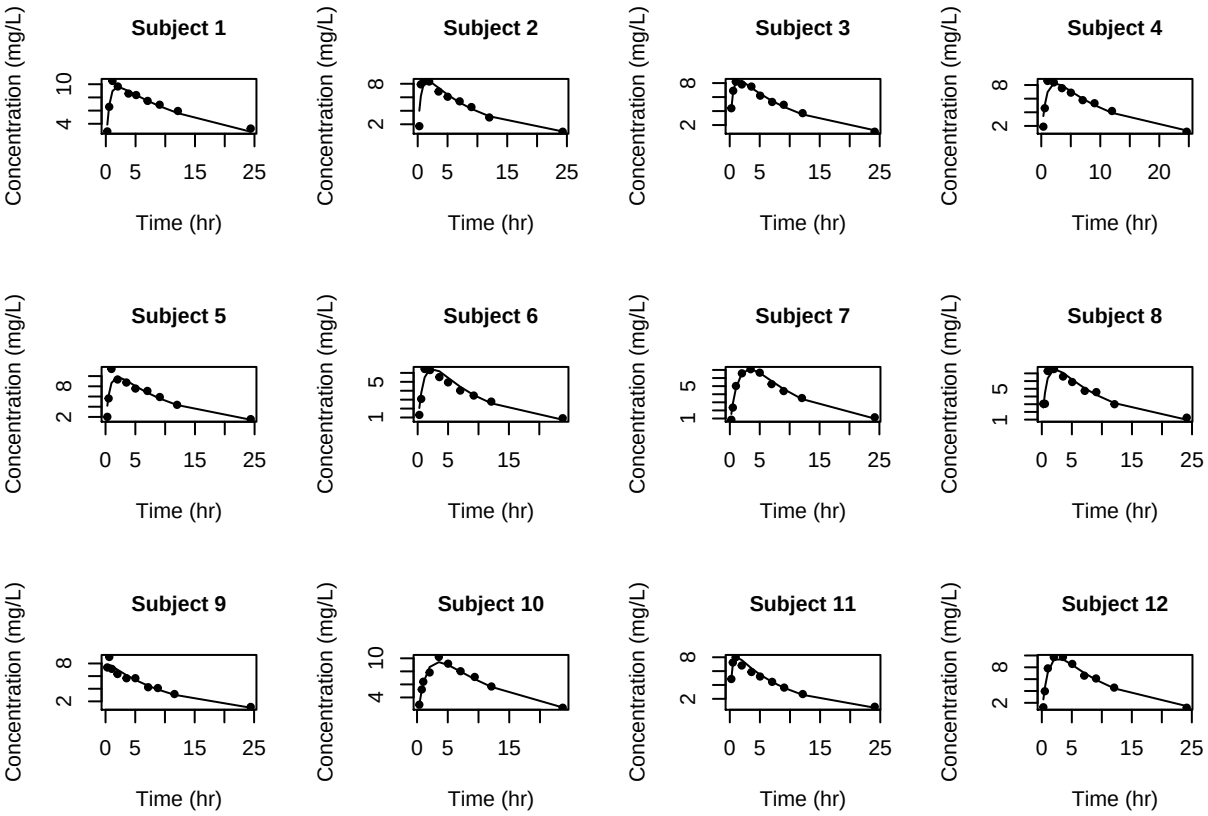

Individual predictions, MAP
Observations
Predictions




```
## 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= 0.06861   (SE= 0.088 )
##        variance= 0.9371   (SE= 0.12 )
##        skewness= 0.9742
##        kurtosis= 2.015
## ------------------------------------------------
## Statistical tests (adjusted p-values):
```

```
##   t-test                : 1
##   Fisher variance test  : 1
##   SW test of normality  : 3.38e-05 ***
##   Global test           : 3.38e-05 ***
## ---
## Signif. codes: '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1
## ------------------------------------------------
```






```
## v Dev mode: OFF
```