Package ‘RxODE’

December 10, 2018

Version 0.8.0-9

Title Facilities for Simulating from ODE-Based Models

Maintainer Wenping Wang <wwang8198@gmail.com>

Depends R (>= 3.3.0)

Suggests knitr, nlme, shiny, tcltk, testthat, devtools, covr, rmarkdown, SnakeCharmR, rSymPy, dplyr, tidyr, tibble, curl, ggplot2, gridExtra, microbenchmark, scales, stringi, htmltools, reticulate

Imports utils, methods, digest, dparser (>= 0.1.8), brew, memoise, magrittr, Rcpp (>= 0.12.3), inline, Matrix, R.utils, PreciseSums (>= 0.3), n1qn1 (>= 6.0.1-2), mvnfast, cli, crayon

Description Facilities for running simulations from ordinary differential equation (ODE) models, such as pharmacometrics and other compartmental models. A compilation manager translates the ODE model into C, compiles it, and dynamically loads the object code into R for improved computational efficiency. An event table object facilitates the specification of complex dosing regimens (optional) and sampling schedules. NB: The use of this package requires both C and Fortran compilers, for details on their use with R please see Section 6.3, Appendix A, and Appendix D in the "R Administration and Installation" manual. Also the code is mostly released under GPL. The VODE and LSODA are in the public domain. The information is available in the inst/COPYRIGHTS.

BugReports https://github.com/nlmixrdevelopment/RxODE/issues

NeedsCompilation yes

VignetteBuilder knitr

License GPL (>= 2)

URL https://www.r-project.org,
https://github.com/nlmixrdevelopment/RxODE

RoxygenNote 6.1.0

LinkingTo dparser(>= 0.1.8), Rcpp (>= 0.12.3), RcppArmadillo(>= 0.5.600.2.0), PreciseSums (>= 0.3)
Author  Matthew L. Fidler [aut],
        Melissa Hallow [aut],
        Wenping Wang [aut, cre],
        Zufar Mulyukov [ctb],
        Justin Wilkins [ctb],
        Simon Frost [ctb],
        Heng Li [ctb],
        Yu Feng [ctb],
        Alan Hindmarsh [ctb],
        Linda Petzold [ctb],
        Ernst Hairer [ctb],
        Gerhard Wanner [ctb],
        Johannes Pfeifer [ctb],
        Robert B. Schnabel [ctb],
        Elizabeth Eskow [ctb],
        J Colinge [ctb],
        Hadley Wickham [ctb],
        G Grothendieck [ctb],
        Robert Gentleman [ctb],
        Ross Ihaka [ctb],
        R core team [cph],
        odepack authors [cph]

Repository  CRAN

Date/Publication  2018-12-10 10:00:07 UTC

R topics documented:

.rxRmPrint  ......................................................... 3
.rxRmSens  ......................................................... 4
.rxRtoolsBaseWin  ................................................... 5
.rxSymPyJacobian  .................................................. 5
.rxWinRtoolsPath  ................................................... 6
add.dosing  ....................................................... 6
add.sampling  ...................................................... 7
cholSE  ........................................................... 8
coef.RxODE  ....................................................... 9
coxBox  .......................................................... 10
cvPost  .......................................................... 10
eventTable  ....................................................... 11
genShinyApp.template  ............................................. 13
is.rxSolve  ....................................................... 15
print.rxCoefSolve  ................................................ 15
print.RxODE  ...................................................... 16
rinvchisq  ....................................................... 16
rxAddReturn  ..................................................... 17
rxAssignPtr  ..................................................... 17
rxChain  .......................................................... 18
Description

Remove print statements
Usage

.rxRmPrint(x)

Arguments

x RxODE lines to remove

Value

RxODE with print lines removed.

Author(s)

Matthew L. Fidler

---

.rxRmSens Remove sensitivity equations

Description

Remove sensitivity equations

Usage

.rxRmSens(x)

Arguments

x RxODE lines to remove

Value

Lines with d/dt(rx_sens_{...}) removed.

Author(s)

Matthew L. Fidler
.rxRtoolsBaseWin | Return Rtools base

Description
Return Rtools base

Usage
.rxRtoolsBaseWin()

Value
Rtools base path, or "" on unix-style platforms.

Author(s)
Matthew L. Fidler

.rxSymPyJacobian | Calculate the full Jacobian for a model

Description
This expand the model to calculate the Jacobian. This requires rSymPy.

Usage
.rxSymPyJacobian(model)

Arguments
model | RxODE family of objects

Value
RxODE syntax for model with Jacobian specified.

Author(s)
Matthew L. Fidler
add.dosing

Description

This adds a dosing event to the event table. This is provided for piping syntax through magrittr

Usage

add.dosing(eventTable, dose, nbr.doses = 1L, dosing.interval = 24, dosing.to = 1L, rate = NULL, amount.units = NA_character_, start.time = 0, do.sampling = FALSE, time.units = NA_character_, ...)  

Arguments

- eventTable: eventTable object
- dose: numeric scalar, dose amount in amount.units;
- nbr.doses: integer, number of doses;
- dosing.interval: required numeric scalar, time between doses in time.units, defaults to 24 of time.units="hours";
- dosing.to: integer, compartment the dose goes into (first compartment by default);
- rate: for infusions, the rate of infusion (default is NULL, for bolus dosing);
add.sampling

### Arguments
- **eventTable**: An `EventTable` object
- **time**: a vector of time values (in `time.units`).
- **time.units**: an optional string specifying the time units. Defaults to the units specified when the `EventTable` was initialized.
- **...**: Other parameters (ignored)

### Value
- `eventTable` with updated sampling. (Note the event table will be updated even if you don’t reassign the `eventTable`)

### Description
This adds a dosing event to the event table. This is provided for piping syntax through magrittr.

### Usage
```r
add.sampling(eventTable, time, time.units = NA, ...)
```

### Author(s)
Matthew L. Fidler

### See Also
- `eventTable`, `RxODE`
cholSE

Author(s)
Matthew L. Fidler

See Also
eventTable, RxODE

cholSE
Generalized Cholesky Matrix Decomposition

Description
Performs a (modified) Cholesky factorization of the form

Usage
cholSE(matrix, tol = (.Machine$double.eps)^((1/3))

Arguments
matrix Matrix to be Factorized.
tol Tolerance; Algorithm suggests (.Machine$double.eps)^(1/3), default

Details
\[ t(P) A P + E = t(R) R \]
As detailed in Schnabel/Eskow (1990)

Value
Generalized Cholesky decomposed matrix.

Note
This version does not pivot or return the E matrix

Author(s)
Matthew L. Fidler (translation), Johannes Pfeifer, Robert B. Schnabel and Elizabeth Eskow

References
matlab source: http://www.dynare.org/dynare-matlab-m2html/matlab/chol_SE.html; Slightly different return values
coef.RxODE  

Return the RxODE coefficients

Description

This returns the parameters, state variables

Usage

```r
## S3 method for class 'RxODE'
coef(object, ...)

## S3 method for class 'RxCompilationManager'
coef(...)

## S3 method for class 'solveRxODE'
coef(object, ...)

## S3 method for class 'rxDll'
coef(...)
```

Arguments

- `object` is an RxODE object
- `...` ignored arguments

Value

a rxCoef object with the following

- `params` is a list of strings for parameters for the RxODE object
- `state` is a list of strings for the names of each state in the RxODE object
- `ini` is the model specified default values for the parameters
- `RxODE` is the referring RxODE object

Author(s)

Matthew L. Fidler
coxBox  

Description

Cox Box transformation

Usage

coxBox(x, lambda = 1)

Arguments

x  data to transform
lambda  Cox-box lambda parameter

Value

Cox-Box Transformed Data

Author(s)

Matthew L. Fidler

cvPost

Description

Sample a covariance Matrix from the Posterior Inverse Wishart distribution.

Note this Inverse wishart rescaled to match the original scale of the covariance matrix.

Usage

cvPost(nu, omega, n = 1L, omegaIsChol = FALSE, returnChol = FALSE)

Arguments

nu  Degrees of Freedom (Number of Observations) for covariance matrix simulation.
omega  Estimate of Covariance matrix.
n  Number of Matrices to sample. By default this is 1.
omegaIsChol  is an indicator of if the omega matrix is in the cholesky decomposition.
returnChol  Return the cholesky decomposition of the covariance matrix sample.
Details

If your covariance matrix is a 1x1 matrix, this uses an scaled inverse chi-squared which is equivalent to the Inverse Wishart distribution in the uni-directional case.

Value

a matrix (n=1) or a list of matrices (n > 1)

Author(s)

Matthew L. Fidler & Wenping Wang

---

**eventTable**

Create an event table object

---

Description

Initializes an object of class ‘EventTable’ with methods for adding and querying dosing and observation records

Usage

`eventTable(amount.units = NA, time.units = "hours")`

Arguments

- **amount.units**
  - string denoting the amount dosing units, e.g., “mg”, “ug”. Default to NA to denote unspecified units. It could also be a solved RxODE object. In that case, eventTable(obj) returns the eventTable that was used to solve the RxODE object.

- **time.units**
  - string denoting the time units, e.g., “hours”, “days”. Default to “hours”.
  - An eventTable is an object that consists of a data.frame storing ordered time-stamped events of an (unspecified) PK/PD dynamic system, units (strings) for dosing and time records, plus a list of functions to add and extract event records.
  - Currently, events can be of two types: dosing events that represent inputs to the system and sampling time events that represent observations of the system with ‘amount.units’ and ‘time.units’, respectively. In the future, additional events may include resetting of state variables (compartments), for instance, to indicate time after “wash-out”, etc.

Value

A closure with the following list of functions:

- `get.EventTable` returns the current event table.
add.dosing  adds dosing records to the event table.
Its arguments are
dose: numeric scalar, dose amount in amount.units;
nbr.doses: integer, number of doses;
dosing.interval: required numeric scalar, time between doses in time.units, 
defaults to 24 of time.units="hours";
dosing.to: integer, compartment the dose goes into (first compartment by de-
default);
rate: for infusions, the rate of infusion (default is NULL, for bolus dosing;
start.time: required dosing start time;
do.sampling: logical, should observation sampling records be added at the 
dosing times? Defaults to FALSE.
amount.units: optional string indicating the dosing units. Defaults to NA to 
indicate as per the original EventTable definition.
time.units: optional string indicating the time units. Defaults to "hours" to 
indicate as per the original EventTable definition.

get.dosing returns a data.frame of dosing records.
clear.dosing clears or deletes all dosing from event table
add.sampling adds sampling time observation records to the event table. Its arguments are
time: a vector of time values (in time.units).
time.units: an optional string specifying the time units. Defaults to the units 
specified when the EventTable was initialized.

get.sampling returns a data.frame of sampled observation records.
clear.sampling removes all sampling from event table.
get.obs.rec returns a logical vector indicating whether each event record represents an ob-
servation or not.
get.nobs returns the number of observation (not dosing) records.
get.units returns a two-element character vector with the dosing and time units, respec-
tively.
copy makes a copy of the current event table. To create a copy of an event table object 
use qd2 <- qd$copy().
expand Expands the event table for multi-subject solving. This is done by qd$expand(400) 
for a 400 subject data expansion

Author(s)
Melissa Hallow and Wenping Wang

See Also
RxODE
Examples

```r
# create dosing and observation (sampling) events
# QD 50mg dosing, 5 days followed by 25mg 5 days
#
qd <- eventTable(amount.units = "mg", time.units = "days")
#
qd$dadd.dosing(dose=50, nbr.doses=5, dosing.interval = 1, do.sampling=FALSE)
#
# sample the system's drug amounts hourly the first day, then every 12 hours
# for the next 4 days
qd$dadd.sampling(seq(from = 0, to = 1, by = 1/24))
qd$dadd.sampling(seq(from = 1, to = 5, by = 12/24))
#
# print(qd$get.dosing())  # table of dosing records
# print(qd$get.nobs())   # number of observation (not dosing) records
#
# BID dosing, 5 days
bid <- eventTable("mg", "days")  # only dosing
bid$dadd.dosing(dose=10000, nbr.doses=2*5,
               dosing.interval = 12, do.sampling=FALSE)
#
# Use the copy() method to create a copy (clone) of an existing
# event table (simple assignments just create a new reference to
# the same event table object (closure)).
#
bid.ext <- bid$copy()  # three-day extension for a 2nd cohort
bid.ext$dadd.dosing(dose = 5000, nbr.doses = 2*3,
              start.time = 120, dosing.interval = 12, do.sampling = FALSE)
#
# You can also use the Piping operator to create a table
qd2 <- eventTable(amount.units="mg", time.units="days") %>%
  add.dosing(dose=50, nbr.doses=5, dosing.interval=1, do.sampling=FALSE) %>%
  add.sampling(seq(from=0, to=1, by=1 / 24)) %>%
  add.sampling(seq(from=1, to=5, by=12 / 24))
# print(qd2$get.dosing())  # table of dosing records
# print(qd2$get.nobs())   # number of observation (not dosing) records
#
# Note that piping with %>% will update the original table.
qd3 <- qd2 %>% add.sampling(seq(from=5, to=10, by=6 / 24))
print(qd2$get.nobs())
print(qd3$get.nobs())
```

Description

Create a complete shiny application for exploring dosing regimens given a (hardcoded) PK/PD model.
Usage

genShinyApp.template(appDir = "shinyExample", verbose = TRUE,
ODE.config = list(ode = "model", params = c(KA = 0.294),
inits = c(ka = 1),
method = "lsoda", atol = 1e-08, rtol = 1e-06))

write.template.server(appDir)

write.template.ui(appDir, statevars)

Arguments

appDir a string with a directory where to store the shiny app, by default is "shinyExample". The directory appDir will be created if it does not exist.

verbose logical specifying whether to write messages as the shiny app is generated. Defaults to TRUE.

ODE.config model name compiled and list of parameters sent to rxSolve.

statevars List of statevars passed to to the write.template.ui function. This usually isn’t called directly.

A PK/PD model is defined using RxODE, and a set of parameters and initial values are defined. Then the appropriate R scripts for the shiny’s user interface ui.R and the server logic server.R are created in the directory appDir.

The function evaluates the following PK/PD model by default:

\[
\begin{align*}
C2 &= \text{centr}/V2; \\
C3 &= \text{peri}/V3; \\
\frac{d}{dt}(\text{depot}) &= -\text{KA}\text{depot}; \\
\frac{d}{dt}(\text{centr}) &= \text{KA}\text{depot} - \text{CL}\text{C2} - Q\text{C2} + Q\text{C3}; \\
\frac{d}{dt}(\text{peri}) &= Q\text{C2} - Q\text{C3}; \\
\frac{d}{dt}(\text{eff}) &= \text{Kin} - K\text{out}*(1-C2/(EC50+C2))\text{eff};
\end{align*}
\]

This can be changed by the ODE.config parameter.

To launch the shiny app, simply issue the runApp(appDir) R command.

Value

None, these functions are used for their side effects.

Note

These functions create a simple, but working example of a dosing regimen simulation web application. Users may want to modify the code to experiment creating shiny applications for their specific RxODE models.

See Also

RxODE.eventTable, and the package shiny (shiny.rstudio.com).
Examples

```r
## Not run:
# create the shiny app example (template)
genShinyApp.template(appDir = "myapp")
# run the shiny app
runApp("myapp")
## End(Not run)
```

is.rxSolve

Check to see if this is an rxSolve object.

Description

Check to see if this is an rxSolve object.

Usage

```r
is.rxSolve(x)
```

Arguments

- `x` object to check to see if it is rxSolve
  
  If this is an rxSolve object that has expired strip all rxSolve information.

Author(s)

Matthew L. Fidler

print.rxCoefSolve

Print the rxCoefSolve object

Description

This prints out the user supplied arguments for the rxCoef object

Usage

```r
## S3 method for class 'rxCoefSolve'
print(x, ...)
```

Arguments

- `x` rxCoefSolve object
  
  `...` Other (ignored) parameters.

Author(s)

Matthew L. Fidler
print.RxODE  Print information about the RxODE object.

Description

This prints the model name and its status for being able to be solved

Usage

## S3 method for class 'RxODE'
print(x, ...)

Arguments

- x: An rxode object
- ...: Ignored parameters

Author(s)

Matthew L. Fidler

rinvchisq  Scaled Inverse Chi Squared distribution

Description

Scaled Inverse Chi Squared distribution

Usage

rinvchisq(n = 1L, nu = 1, scale = 1)

Arguments

- n: Number of random samples
- nu: degrees of freedom of inverse chi square
- scale: Scale of inverse chi squared distribution (default is 1).

Value

A vector of inverse chi squared deviates.
**rxAddReturn**

*Add a return statement to a function.*

**Description**

Add a return statement to a function.

**Usage**

```r
rxAddReturn(fn, ret = TRUE)
```

**Arguments**

- `fn` Function to deparse
- `ret` boolean stating if a return statement will be added.

**Value**

Function with parens removed and add a return statement.

**Author(s)**

Matthew L. Fidler

---

**rxAssignPtr**

*Assign pointer based on model variables*

**Description**

Assign pointer based on model variables

**Usage**

```r
rxAssignPtr(object = NULL)
```

**Arguments**

- `object` RxODE family of objects
**rxChain**

**rxChain Chain or add item to solved system of equations**

**Description**

Add item to solved system of equations

**Usage**

```
rxChain(obj1, obj2)
```

```
## S3 method for class 'solveRxDll'
obj1 + obj2
```

**Arguments**

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>obj1</td>
<td>Solved object.</td>
</tr>
<tr>
<td>obj2</td>
<td>New object to be added/piped/chained to solved object.</td>
</tr>
</tbody>
</table>

**Value**

When `newObject` is an event table, return a new solved object with the new event table.

**Author(s)**

Matthew L. Fidler

---

**rxClean**

**Cleanup anonymous DLLs**

**Description**

This cleans up any DLLs created by text files

**Usage**

```
rxClean(wd)
```

**Arguments**

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>wd</td>
<td>What directory should be cleand</td>
</tr>
</tbody>
</table>

This cleans up all files named `rx-*.dll` and associated files as well as `call_dvode.o` and associated files.
Value
TRUE if successful

Author(s)
Matthew L. Fidler

Description
This is the compilation workhorse creating the RxODE model DLL files.

Usage
rxCompile(model, dir, prefix, extraC = NULL, force = FALSE,
modName = NULL, calcJac = NULL, calcSens = NULL,
collapseModel = FALSE, ...)

## S3 method for class 'character'
rxCompile(model, dir = NULL, prefix = NULL,
extraC = NULL, force = FALSE, modName = NULL, calcJac = NULL,
calcSens = NULL, collapseModel = FALSE, ...)

## S3 method for class 'rxDll'
rxCompile(model, ...)

## S3 method for class 'RxODE'
rxCompile(model, ...)

Arguments
model This is the ODE model specification. It can be:
• a string containing the set of ordinary differential equations (ODE) and
  other expressions defining the changes in the dynamic system.
• a file name where the ODE system equation is contained
• An ODE expression enclosed in {} (see also the filename argument). For details, see the sections “Details” and
  “RxODE Syntax” below.
dir This is the model directory where the C file will be stored for compiling.
If unspecified, the C code is stored in a temporary directory, then the model is
compiled and moved to the current directory. Afterwards the C code is removed.
If specified, the C code is stored in the specified directory and then compiled in
that directory. The C code is not removed after the DLL is created in the same
directory. This can be useful to debug the c-code outputs.
prefix is a string indicating the prefix to use in the C based functions. If missing, it is calculated based on file name, or md5 of parsed model.

extraC Extra c code to include in the model. This can be useful to specify functions in the model. These C functions should usually take double precision arguments, and return double precision values.

force is a boolean stating if the (re)compile should be forced if RxODE detects that the models are the same as already generated.

modName a string to be used as the model name. This string is used for naming various aspects of the computations, including generating C symbol names, dynamic libraries, etc. Therefore, it is necessary that modName consists of simple ASCII alphanumeric characters starting with a letter.

calcJac boolean indicating if RxODE will calculate the Jacobain according to the specified ODEs.

calcSens boolean indicating if RxODE will calculate the sensitivities according to the specified ODEs.

collapseModel boolean indicating if RxODE will remove all LHS variables when calculating sensitivities.

... Other arguments sent to the rxTrans function.

Value

An rxDll object that has the following components

dll DLL path

model model specification

.c A function to call C code in the correct context from the DLL using the .C function.

.call A function to call C code in the correct context from the DLL using the .Call function.

args A list of the arguments used to create the rxDll object.

Author(s)

Matthew L.Fidler

See Also

RxODE
rxCores

Get the number of cores in a system

Description

Get the number of cores in a system

Usage

rxCores()

rxDelete

Delete the DLL for the model

Description

This function deletes the DLL, but doesn’t delete the model information in the object.

Usage

rxDelete(obj)

Arguments

obj RxODE family of objects

Value

A boolean stating if the operation was successful.

Author(s)

Matthew L. Fidler
**rxdfdy**

*Jacobian and parameter derivatives*

---

**Description**

Return Jacobian and parameter derivatives

**Usage**

```
rxdfdy(obj)
```

**Arguments**

- `obj` : RxODE family of objects

**Value**

A list of the jacobian parameters defined in this RxODE object.

**Author(s)**

Matthew L. Fidler

---

**rxfoexpandeta**

*First Order Expansion of ETA*

---

**Description**

First Order Expansion of ETA

**Usage**

```
rxfoexpandeta(expr)
```

**Arguments**

- `expr` : RxODE model

**Value**

Return a RxODE model with first order Taylor expansion around ETA

**Author(s)**

Matthew L. Fidler
**rxGetRxODE**

Get RxODE model from object

**Description**
Get RxODE model from object

**Usage**
rxGetRxODE(obj)

**Arguments**

- obj
  - RxODE family of objects

---

**rxHtml**
Format rxSolve and related objects as html.

**Description**
Format rxSolve and related objects as html.

**Usage**
rxHtml(x, ...)

```
## S3 method for class 'rxSolve'
rxHtml(x, ...)
```

**Arguments**

- x
  - RxODE object
- ...  
  - Extra arguments sent to kable

**Author(s)**
Matthew L. Fidler
**rxInv**

Invert matrix using Rcpp Armadillo.

**Description**

Invert matrix using Rcpp Armadillo.

**Usage**

(rxInv(matrix)

**Arguments**

matrix matrix to be inverted.

**Value**

inverse or pseudo inverse of matrix.

**rxIsCurrent**

Checks if the RxODE object was built with the current build

**Description**

Checks if the RxODE object was built with the current build

**Usage**

rxIsCurrent(obj)

**Arguments**

obj RxODE family of objects

**Value**

boolean indicating if this was built with current RxODE
**rxLhs**  
*Left handed Variables*

**Description**  
This returns the model calculated variables

**Usage**  
```r
rxLhs(obj)
```

**Arguments**  
- **obj**  
  RxODE family of objects

**Value**  
A character vector listing the calculated parameters

**Author(s)**  
Matthew L.Fidler

**See Also**  
- `rxode`
- `rxnorm`

---

**rxNorm**  
*Get the normalized model*

**Description**  
This get the syntax prefered model for processing

**Usage**  
```r
rxNorm(obj, condition = NULL, removeInis, removeJac, removeSens)
```

**Arguments**  
- **obj**  
  RxODE family of objects
- **condition**  
  Character string of a logical condition to use for subsetting the normalized model. When missing, and a condition is not set via `rxCondition`, return the whole code with all the conditional settings intact. When a condition is set with `rxCondition`, use that condition.
- **removeInis**  
  A boolean indicating if parameter initializations will be removed from the model
- **removeJac**  
  A boolean indicating if the Jacobians will be removed.
- **removeSens**  
  A boolean indicating if the sensitivities will be removed.
Value

Normalized Normal syntax (no comments)

Author(s)

Matthew L. Fidler

---

RxODE

*Create an ODE-based model specification*

---

Description

Create a dynamic ODE-based model object suitably for translation into fast C code

Usage

```r
RxODE(model, modName = basename(wd), wd = ifelse(RxODE.cache.directory
== ".", getwd(), RxODE.cache.directory), filename = NULL,
extraC = NULL, debug = FALSE, calcJac = NULL, calcSens = NULL,
collapseModel = FALSE, ...)  
```

Arguments

- **model**: This is the ODE model specification. It can be:
  - a string containing the set of ordinary differential equations (ODE) and other expressions defining the changes in the dynamic system.
  - a file name where the ODE system equation is contained
  - An ODE expression enclosed in {}
  (see also the filename argument). For details, see the sections “Details” and “rxode Syntax” below.
- **modName**: a string to be used as the model name. This string is used for naming various aspects of the computations, including generating C symbol names, dynamic libraries, etc. Therefore, it is necessary that modName consists of simple ASCII alphanumeric characters starting with a letter.
- **wd**: character string with a working directory where to create a subdirectory according to modName. When specified, a subdirectory named after the “modName.d” will be created and populated with a C file, a dynamic loading library, plus various other working files. If missing, the files are created (and removed) in the temporary directory, and the RxODE DLL for the model is created in the current directory named `rx_????_platform`, for example `rx_129f8f97fb94a87ca49ca8dafa691e1e_i386.dll`.
- **filename**: A file name or connection object where the ODE-based model specification resides. Only one of model or filename may be specified.
- **extraC**: Extra c code to include in the model. This can be useful to specify functions in the model. These C functions should usually take double precision arguments, and return double precision values.
debug is a boolean indicating if the executable should be compiled with verbose debugging information turned on.

calcJac boolean indicating if RxODE will calculate the Jacobian according to the specified ODEs.

calcSens boolean indicating if RxODE will calculate the sensitivities according to the specified ODEs.

collapseModel boolean indicating if RxODE will remove all LHS variables when calculating sensitivities.

... any other arguments are passed to the function `readLines`, (e.g., encoding).

The “Rx” in the name `rxode` is meant to suggest the abbreviation RX for a medical prescription, and thus to suggest the package emphasis on pharmacometrics modeling, including pharmacokinetics (PK), pharmacodynamics (PD), disease progression, drug-disease modeling, etc.

The ODE-based model specification may be coded inside a character string or in a text file, see Section `RxODE Syntax` below for coding details. An internal `rxode` compilation manager object translates the ODE system into C, compiles it, and dynamically loads the object code into the current R session. The call to `rxode` produces an object of class `rxode` which consists of a list-like structure (closure) with various member functions (see Section `Value` below).

For evaluating `RxODE` models, two types of inputs may be provided: a required set of time points for querying the state of the ODE system and an optional set of doses (input amounts). These inputs are combined into a single `event table` object created with the function `eventTable`.

Value

An object (closure) of class “RxODE” (see Chambers and Temple Lang (2001)) consisting of the following list of strings and functions:

- `modName` the name of the model (a copy of the input argument).
- `model` a character string holding the source model specification.
- `get.modelVars` a function that returns a list with 3 character vectors, `params`, `state`, and `lhs` of variable names used in the model specification. These will be output when the model is computed (i.e., the ODE solved by integration).
- `solve` this function solves (integrates) the ODE. This is done by passing the code to `rxSolve`. This is as if you called `rxSolve`(`RxODEobject`, ...), but returns a matrix instead of a `rxSolve` object.

- `params`: a numeric named vector with values for every parameter in the ODE system; the names must correspond to the parameter identifiers used in the ODE specification;
- `events`: an `eventTable` object describing the input (e.g., doses) to the dynamic system and observation sampling time points (see `eventTable`);
- `inits`: a vector of initial values of the state variables (e.g., amounts in each compartment), and the order in this vector must be the same as the state variables (e.g., PK/PD compartments);
stiff: a logical (TRUE by default) indicating whether the ODE system is stiff or not.

For stiff ODE systems (stiff = TRUE), RxODE uses the LSODA (Livermore Solver for Ordinary Differential Equations) Fortran package, which implements an automatic method switching for stiff and non-stiff problems along the integration interval, authored by Hindmarsh and Petzold (2003).

For non-stiff systems (stiff = FALSE), RxODE uses DOP853, an explicit Runge-Kutta method of order 8(5, 3) of Dormand and Prince as implemented in C by Hairer and Wanner (1993).

trans_abs: a logical (FALSE by default) indicating whether to fit a transit absorption term (TODO: need further documentation and example);
atol: a numeric absolute tolerance (1e-08 by default);
rtol: a numeric relative tolerance (1e-06 by default).

The output of “solve” is a matrix with as many rows as there are sampled time points and as many columns as system variables (as defined by the ODEs and additional assignments in the RxODE model code).

isValid a function that (naively) checks for model validity, namely that the C object code reflects the latest model specification.

version a string with the version of the RxODE object (not the package).
dynLoad a function with one force = FALSE argument that dynamically loads the object code if needed.
dynUnload a function with no argument that unloads the model object code.
delete removes all created model files, including C and DDL files. The model object is no longer valid and should be removed, e.g., rm(m1).

run deprecated, use solve.
parse deprecated.
compile deprecated.
get.index deprecated.
getObj internal (not user callable) function.

RxODE Syntax

An RxODE model specification consists of one or more statements terminated by semi-colons, ‘;’, and optional comments (comments are delimited by # and an end-of-line marker). NB: Comments are not allowed inside statements.

A block of statements is a set of statements delimited by curly braces, ‘{ ... }’. Statements can be either assignments or conditional if statements. Assignment statements can be: (1) “simple” assignments, where the left hand is an identifier (i.e., variable), (2) special “time-derivative” assignments, where the left hand specifies the change of that variable with respect to time e.g., d/dt(depot), or (3) special “jacobian” assignments, where the left hand specifies the change of of the ODE with respect to one of the parameters, e.g. df(depot)/dy(ke1). The “jacobian” assignments are not required, and are only useful for very stiff differential systems.

Expressions in assignment and ‘if’ statements can be numeric or logical (no character expressions are currently supported). Numeric expressions can include the following numeric operators (“+”, “-”, “*”, “/”, “^”), and logical operators (“&”, “|”, “!”).
Identifiers in an RxODE model specification can refer to:

- state variables in the dynamic system (e.g., compartments in a pharmacokinetics/pharmacodynamics model);
- implied input variable, \( t \) (time), \( podo \) (oral dose, for absorption models), and \( t_{\text{last}} \) (last time point);
- model parameters, (\( ka \) rate of absorption, \( CL \) clearance, etc.);
- \( \pi \), for the constant \( \pi \).
- others, as created by assignments as part of the model specification.

Identifiers consists of case-sensitive alphanumeric characters, plus the underscore `_` character. **NB:** the dot `_` character is **not** a valid character identifier.

The values of these variables at pre-specified time points are saved as part of the fitted/integrated/solved model (see `eventTable`, in particular its member function `addNsampling` that defines a set of time points at which to capture a snapshot of the system via the values of these variables).

The ODE specification mini-language is parsed with the help of the open source tool DParser, Plevyak (2015).

**Author(s)**

Melissa Hallow, Wenping Wang and Matthew Fidler

**References**


**See Also**

`eventTable`

**Examples**

```r
# Step 1 - Create a model specification
ode <- "
# A 4-compartment model, 3 PK and a PD (effect) compartment
# (notice state variable names 'depot', 'centr', 'peri', 'eff')
```

C2 = centr/V2;
C3 = peri/V3;
d/dt(depot) = KA*depot;
d/dt(centr) = KA*depot - CL*C2 - Q*C2 + Q*C3;
d/dt(peri) = Q*C2 - Q*C3;
d/dt(eff) = Kin - Kout*(1-C2/(EC50+C2))*eff;

m1 <- RxODE(model = ode, modName = "m1")
print(m1)

# Step 2 - Create the model input as an EventTable,
# including dosing and observation (sampling) events

# QD (once daily) dosing for 5 days.
qd <- eventTable(amount.units = "ug", time.units = "hours")
qd$add.dosing(dose = 10000, nbr.doses = 5, dosing.interval = 24)

# Sample the system hourly during the first day, every 8 hours
# then after
qd$sampling(0:24)
qd$sampling(seq(from = 24+8, to = 5*24, by = 8))

# Step 3 - set starting parameter estimates and initial
# values of the state
theta <-
c(KA = .291, CL = 18.6,
   V2 = 40.2, Q = 10.5, V3 = 297.0,
   Kin = 1.0, Kout = 1.0, EC50 = 200.0)

# init state variable
inits <- c(0, 0, 1, 0);

# Step 4 - Fit the model to the data
qd.cp <- m1$solve(theta, events = qd, inits)

head(qd.cp)

# This returns a matrix. Note that you can also
# solve using name initial values. For example:
inits <- c(eff = 1);
qd.cp <- solve(m1, theta, events = qd, inits);

---

Optimize RxODE for computer evaluation
**rxOptions**

**Description**

This optimizes RxODE code for computer evaluation by only calculating redundant expressions once.

**Usage**

\[ rxOptExpr(x) \]

**Arguments**

- \( x \) RxODE model that can be access by rxNorm

**Value**

Optimized RxODE model text. The order and type lhs and state variables is maintained while the evaluation is sped up. While parameters names are maintained, their order may be modified.

**Author(s)**

Matthew L. Fidler

---

**rxOptions**

Options for RxODE

**Description**

This is a backend for rxPermissive (with \( op.rx = 2 \)) and rxStrict (with \( op.rx = 1 \))

**Usage**

\[ rxOptions(expr, op.rx = NULL, silent = .isTestthat(), respect = FALSE, rxclean = .isTestthat(), cran = FALSE, on.validate = FALSE) \]

**Arguments**

- \( expr \) Expression to evaluate in the permissive/strict environment. If unspecified, set the options for the current environment.
- \( op.rx \) A numeric for strict (1) or permissive (2) syntax.
- \( silent \) when true, also silence the syntax errors and interactive output (useful in testing).
- \( respect \) when TRUE, respect any options that are specified. This is called at startup, but really should not be called elsewhere, otherwise the options are not changed.
- \( rxclean \) when TRUE, call rxClean before and after the expr is called.
- \( cran \) When specified and true, run on CRAN. Otherwise it is skipped on cran.
- \( on.validate \) When TRUE run only when validating.
Details

When `expr` is missing and `op.rx` is NULL, this displays the current RxODE options.

Author(s)

Matthew L. Fidler

---

```r
rxParams
```

### Parameters specified by the model

---

Description

This return the model’s parameters that are required to solve the ODE system.

Usage

```r
rxParams(obj, constants = TRUE)
```

```r
rxParam(obj, constants = TRUE)
```

Arguments

- `obj` RxODE family of objects
- `constants` is a boolean indicating if constants should be included in the list of parameters. Currently RxODE parses constants into variables in case you wish to change them without recompiling the RxODE model.

Value

a character vector listing the parameters in the model.

Author(s)

Matthew L. Fidler
### rxPermissive

**Permissive or Strict RxODE syntax options**

**Description**

This sets the RxODE syntax to be permissive or strict.

**Usage**

```r
rxPermissive(expr, silent = .isTestthat(), respect = FALSE, 
              rxclean = .isTestthat(), cran = FALSE, on.validate = FALSE)
```

```r
rxStrict(expr, silent = .isTestthat(), respect = FALSE, 
          rxclean = .isTestthat(), cran = FALSE, on.validate = FALSE)
```

**Arguments**

- **expr**: Expression to evaluate in the permissive/strict environment. If unspecified, set the options for the current environment.
- **silent**: when true, also silence the syntax errors and interactive output (useful in testing).
- **respect**: when TRUE, respect any options that are specified. This is called at startup, but really should not be called elsewhere, otherwise the options are not changed.
- **rxclean**: when TRUE, call rxClean before and after the expr is called.
- **cran**: When specified and true, run on CRAN. Otherwise it is skipped on cran.
- **on.validate**: When TRUE run only when validating.

**Author(s)**

Matthew L. Fidler

### rxProgress

**RxODE progress bar functions**

**Description**

`rxProgress` sets up the progress bar.

**Usage**

```r
rxProgress(num, core = 0L)
```

```r
rxTick()
```

```r
rxProgressStop(clear = TRUE)
```

```r
rxProgressAbort()
```
Arguments

num  Tot number of operations to track
core Number of cores to show. If below 1, don’t show number of cores
clear Boolean telling if you should clear the progress bar after completion (as if it wasn’t displayed). By default this is TRUE

Details

rxTick is a progress bar tick
rxProgressStop stop progress bar
rxProgressAbort shows an abort if rxProgressStop wasn’t called.

Value

All return NULL invisibly.

Author(s)

Matthew L. Fidler

Examples

f <- function(){
on.exit((rxProgressAbort()));
rxProgress(100)
  for (i in 1:100) {
    rxTick()
    Sys.sleep(1 / 100)
  }
  rxProgressStop();
}

## Not run:
f();

## End(Not run)

| rxSetProd | Choose the type of product to use in RxODE. These are used in the RxODE prod blocks |

Description

Choose the type of product to use in RxODE. These are used in the RxODE prod blocks
**rxSetSum**

**Usage**

```r
rxSetProd(type = c("long double", "double", "logify"))
```

**Arguments**

- `type`: Product to use for `prod()` in RxODE blocks
  - `long double`: Converts to long double, performs the multiplication and then converts back.
  - `double`: Uses the standard double scale for multiplication.

**Value**

- `nothing`

**Author(s)**

- Matthew L. Fidler

---

**rxSetSum**

Choose the type of sums to use for RxODE.

**Description**

Choose the types of sums to use in RxODE. These are used in the RxODE `sum` blocks and the `rxSum` function.

**Usage**

```r
rxSetSum(type = c("pairwise", "fsum", "kahan", "neumaier", "c"))
```

**Arguments**

- `type`: Sum type to use for `rxSum` and `sum()` in RxODE code blocks.
  - `pairwise`: Uses the pairwise sum (fast, default)
  - `fsum`: Uses Python’s `fsum` function (most accurate)
  - `kahan`: Uses kahan correction
  - `neumaier`: Uses Neumaier correction
  - `c`: Uses no correction, but default/native summing

**Value**

- `nothing`

**Author(s)**

- Matthew L. Fidler
Description

Use Shiny to help develop an RxODE model

Usage

```r
rxShiny(object, params = c(), events = NULL, inits = c(), ..., data = data.frame())

## S3 method for class 'rxSolve'
rxShiny(object, params = NULL, events = NULL,
         inits = c(), ..., data = data.frame())

## Default S3 method:
rxShiny(object = NULL, params = c(), events = NULL,
        inits = c(), ..., data = data.frame())
```

Arguments

- **object**: A RxODE family of objects. If not supplied a 2-compartment indirect effect model is used. If it is supplied, use the model associated with the RxODE object for the model exploration.
- **params**: Initial parameters for model
- **events**: Event information (currently ignored)
- **inits**: Initial estimates for model
- **...**: Other arguments passed to rxShiny. Currently doesn’t do anything.
- **data**: Any data that you would like to plot. If the data has a time variable as well as a compartment or calculated variable that matches the RxODE model, the data will be added to the plot of a specific compartment or calculated variable.

Value

Nothing; Starts a shiny server

Author(s)

Zufar Mulyukov and Matthew L. Fidler
rxSimThetaOmega

Simulate Parameters from a Theta/Omega specification

Description

Simulate Parameters from a Theta/Omega specification

Usage

rxSimThetaOmega(params = NULL, omega = NULL, omegaDf = NULL, omegaIsChol = FALSE, nSub = 1L, thetaMat = NULL, thetaDf = NULL, thetaIsChol = FALSE, nStud = 1L, sigma = NULL, sigmaDf = NULL, sigmaIsChol = FALSE, nCoresRV = 1L, nObs = 1L, dfSub = 0, dfObs = 0, simSubjects = TRUE)

Arguments

params Named Vector of RxODE model parameters
omega Named omega matrix.
omegaDf The degrees of freedom of a t-distribution for simulation. By default this is NULL which is equivalent to Inf degrees, or to simulate from a normal distribution instead of a t-distribution.
omegaIsChol Indicates if the omega supplied is a Cholesky decomposed matrix instead of the traditional symmetric matrix.
nSub Number between subject variabilities (ETAs) simulated for every realization of the parameters.
thetaMat Named theta matrix.
thetaDf The degrees of freedom of a t-distribution for simulation. By default this is NULL which is equivalent to Inf degrees, or to simulate from a normal distribution instead of a t-distribution.
thetaIsChol Indicates if the theta supplied is a Cholesky decomposed matrix instead of the traditional symmetric matrix.
nStud Number virtual studies to characterize uncertainty in estimated parameters.
sigma Matrix for residual variation. Adds a "NA" value for each of the indivdual parameters, residuals are updated after solve is completed.
sigmaDf Degrees of freedom of the sigma t-distribution. By default it is equivalent to Inf, or a normal distribution.
sigmaIsChol Boolean indicating if the sigma is in the Cholesky decomposition instead of a symmetric covariance
nCoresRV Number of cores used for the simulation of the sigma variables. By default this is 1. This uses the package rmvn and rmvt. To reproduce the results you need to run on the same platform with the same number of cores. This is the reason this is set to be one, regardless of what the number of cores are used in threaded ODE solving.
Number of observations to simulate (with sigma matrix)

Degrees of freedom to sample the between subject variability matrix from the inverse Wishart distribution (scaled) or scaled inverse chi squared distribution.

Degrees of freedom to sample the unexplained variability matrix from the inverse Wishart distribution (scaled) or scaled inverse chi squared distribution.

boolean indicated RxODE should simulate subjects in studies (TRUE, default) or studies (FALSE)

**Author(s)**

Matthew L. Fidler

---

**rxSolve**

*Solves a ODE equation*

**Description**

This uses RxODE family of objects, file, or model specification to solve a ODE system.

**Usage**

```r
rxSolve(object, ...)  
## Default S3 method:
rxSolve(object, params = NULL, events = NULL,  
inits = NULL, scale = NULL, covs = NULL, method = c("liblsoda",  
"lsoda", "dop853"), transitAbs = NULL, atol = 1e-08, rtol = 1e-06,  
maxsteps = 5000L, hmin = 0L, hmax = NULL, hini = 0L,  
maxordn = 12L, maxords = 5L, ..., cores,  
covsInterpolation = c("locf", "linear", "nocb", "midpoint"),  
addCov = FALSE, matrix = FALSE, sigma = NULL, sigmadf = NULL,  
nCoresRV = 1L, sigmaIsChol = FALSE, nDisplayProgress = 10000L,  
amountUnits = NA_character_, timeUnits = "hours", stiff,  
theta = NULL, eta = NULL, addDosing = FALSE, stateTrim = Inf,  
updateObject = FALSE, doSolve = TRUE, omega = NULL,  
omegadf = NULL, omegasIsChol = FALSE, nSub = 1L, thetaMat = NULL,  
thetaDf = NULL, thetaIsChol = FALSE, nStud = 1L, dfSub = 0,  
dfObs = 0, returnType = c("rxSolve", "matrix", "data.frame",  
"data.frame.TBS"), seed = NULL, nsim = NULL, setupOnly = FALSE)  
## S3 method for class 'rxSolve'
update(object, ...)  
## S3 method for class 'RxODE'
predict(object, ...)
```
## Arguments

**object**

is a either a RxODE family of objects, or a file-name with a RxODE model specification, or a string with a RxODE model specification.

**...**

Other arguments including scaling factors for each compartment. This includes $S# = \text{numeric}$ will scale a compartment # by a dividing the compartment amount by the scale factor, like NONMEM.

**params**

a numeric named vector with values for every parameter in the ODE system; the names must correspond to the parameter identifiers used in the ODE specification;

**events**

an \texttt{eventTable} object describing the input (e.g., doses) to the dynamic system and observation sampling time points (see \texttt{eventTable});

**inits**

a vector of initial values of the state variables (e.g., amounts in each compartment), and the order in this vector must be the same as the state variables (e.g., PK/PD compartments);

**scale**

a numeric named vector with scaling for ode parameters of the system. The names must correspond to the parameter identifiers in the ODE specification. Each of the ODE variables will be divided by the scaling factor. For example \texttt{scale=(center=2)} will divide the center ODE variable by 2.

**covs**

a matrix or dataframe the same number of rows as the sampling points defined in the events \texttt{eventTable}. This is for time-varying covariates.

**method**

The method for solving ODEs. Currently this supports:

- "liblsoda" thread safe lsoda. This supports parallel thread-based solving, and ignores user Jacobian specification.
- "lsoda" – LSODA solver. Does not support parallel thread-based solving, but allows user Jacobian specification.

**transitAbs**

boolean indicating if this is a transit compartment absorption
atol  a numeric absolute tolerance (1e-8 by default) used by the ODE solver to determine if a good solution has been achieved; This is also used in the solved linear model to check if prior doses do not add anything to the solution.

rtol  a numeric relative tolerance (1e-6 by default) used by the ODE solver to determine if a good solution has been achieved. This is also used in the solved linear model to check if prior doses do not add anything to the solution.

maxsteps  maximum number of (internally defined) steps allowed during one call to the solver. (5000 by default)

hmin  The minimum absolute step size allowed. The default value is 0.

hmax  The maximum absolute step size allowed. The default checks for the maximum difference in times in your sampling and events, and uses this value. The value 0 is equivalent to infinite maximum absolute step size.

hini  The step size to be attempted on the first step. The default value is determined by the solver (when hini = 0)

maxordn  The maximum order to be allowed for the nonstiff (Adams) method. The default is 12. It can be between 1 and 12.

maxords  The maximum order to be allowed for the stiff (BDF) method. The default value is 5. This can be between 1 and 5.

cores  Number of cores used in parallel ODE solving. This defaults to the number or system cores determined by rxCores for methods that support parallel solving (ie thread-safe methods like "liblsoda").

covsInterpolation  specifies the interpolation method for time-varying covariates. When solving ODEs it often samples times outside the sampling time specified in events. When this happens, the time varying covariates are interpolated. Currently this can be:

- "linear" interpolation (the default), which interpolates the covariate by solving the line between the observed covariates and extrapolating the new covariate value.
- "constant" – Last observation carried forward.
- "NOCB" – Next Observation Carried Backward. This is the same method that NONMEM uses.
- "midpoint" Last observation carried forward to midpoint; Next observation carried backward to midpoint.

addCov  A boolean indicating if covariates should be added to the output matrix or data frame. By default this is disabled.

matrix  A boolean indicating if a matrix should be returned instead of the RxODE’s solved object.

sigma  Named sigma covariance or Cholesky decomposition of a covariance matrix. The names of the columns indicate parameters that are simulated. These are simulated for every observation in the solved system.

sigmaDf  Degrees of freedom of the sigma t-distribution. By default it is equivalent to Inf, or a normal distribution.
nCoresRV

Number of cores used for the simulation of the sigma variables. By default this is 1. This uses the package rmvn and rmvt. To reproduce the results you need to run on the same platform with the same number of cores. This is the reason this is set to be one, regardless of what the number of cores are used in threaded ODE solving.

sigmaIsChol

Boolean indicating if the sigma is in the Cholesky decomposition instead of a symmetric covariance

nDisplayProgress

An integer indicating the minimum number of c-based solves before a progress bar is shown. By default this is 10,000.

amountUnits

This supplies the dose units of a data frame supplied instead of an event table. This is for importing the data as an RxODE event table.

timeUnits

This supplies the time units of a data frame supplied instead of an event table. This is for importing the data as an RxODE event table.

stiff

a logical (TRUE by default) indicating whether the ODE system is stiff or not.

For stiff ODE systems (stiff = TRUE), RxODE uses the LSODA (Livermore Solver for Ordinary Differential Equations) Fortran package, which implements an automatic method switching for stiff and non-stiff problems along the integration interval, authored by Hindmarsh and Petzold (2003).

For non-stiff systems (stiff = FALSE), RxODE uses DOP853, an explicit Runge-Kutta method of order 8(5, 3) of Dormand and Prince as implemented in C by Hairer and Wanner (1993).

theta

A vector of parameters that will be named THETA[##] and added to parameters

eta

A vector of parameters that will be named ETA[##] and added to parameters

addDosing

Boolean indicating if the solve should add RxODE evid and amt columns. This will also include dosing information and estimates at the doses. Be default, RxODE only includes estimates at the observations. (default FALSE).

stateTrim

When amounts/concentrations in one of the states are above this value, trim them to be this value. By default Inf. Also trims to -stateTrim for lage negative amounts/concentrations

updateObject

This is an internally used flag to update the RxODE solved object (when supplying an RxODE solved object) as well as returning a new object. You probably should not modify it’s FALSE default unless you are willing to have unexpected results.

doSolve

Internal flag. By default this is TRUE, when FALSE a list of solving options is returned.

omega

Named omega matrix.

omegaDF

The degrees of freedom of a t-distribution for simulation. By default this is NULL which is equivalent to Inf degrees, or to simulate from a normal distribution instead of a t-distribution.

omegaIsChol

Indicates if the omega supplied is a Cholesky decomposed matrix instead of the traditional symmetric matrix.

nSub

Number between subject variabilities (ETAs) simulated for every realization of the parameters.
thetaMat  Named theta matrix.
thetaDf   The degrees of freedom of a t-distribution for simulation. By default this is NULL which is equivalent to Inf degrees, or to simulate from a normal distribution instead of a t-distribution.
thetaIsChol Indicates if the theta supplied is a Cholesky decomposed matrix instead of the traditional symmetric matrix.
nStud Number virtual studies to characterize uncertainty in estimated parameters.
dfSub Degrees of freedom to sample the between subject variability matrix from the inverse Wishart distribution (scaled) or scaled inverse chi squared distribution.
dfObs Degrees of freedom to sample the unexplained variability matrix from the inverse Wishart distribution (scaled) or scaled inverse chi squared distribution.
returnType This tells what type of object is returned. The currently supported types are:
  * "rxSolve" (default) will return a reactive data frame that can change easily change different pieces of the solve and update the data frame. This is the currently standard solving method in RxODE, is used for \texttt{rxSolve(object, ...), solve(object,...)},
  * "data.frame" – returns a plain, non-reactive data frame. Currently very slightly Faster than returnType="matrix"
  * "matrix" – returns a plain matrix with column names attached to the solved object. This is what is used \texttt{object$run} as well as \texttt{object$solve}
seed an object specifying if and how the random number generator should be initialized
nsim represents the number of simulations. For RxODE, if you supply single subject event tables (created with eventTable)
setupOnly Only setup the internal C structure, do not solve. After setting it up, and using the structure in C, it needs to be freed by \texttt{rxSolveFree}.
a when using solve, this is equivalent to the object argument. If you specify object later in the argument list it overwrites this parameter.
b when using solve, this is equivalent to the params argument. If you specify params as a named argument, this overwrites the output

Value

An “rxSolve” solve object that stores the solved value in a matrix with as many rows as there are sampled time points and as many columns as system variables (as defined by the ODEs and additional assignments in the RxODE model code). It also stores information about the call to allow dynamic updating of the solved object.

The operations for the object are similar to a data-frame, but expand the \$ and [[""]] access operators and assignment operators to resolve based on different parameter values, initial conditions, solver parameters, or events (by updating the time variable).

You can call the \texttt{eventTable} methods on the solved object to update the event table and resolve the system of equations.
Author(s)

Matthew Fidler, Melissa Hallow and Wenping Wang

References


See Also

`rxode`

---

**rxState**

*State variables*

**Description**

This returns the model’s compartments or states.

**Usage**

```r
rxState(obj = NULL, state = NULL)
```

**Arguments**

- `obj` RxDRE family of objects
- `state` is a string indicating the state or compartment that you would like to lookup.

**Value**

If state is missing, return a character vector of all the states.

If state is a string, return the compartment number of the named state.

**Author(s)**

Matthew L.Fidler

See Also

`rxODE`
**rxSumProdModel**  
*Recast model in terms of sum/prod*

**Description**  
Recast model in terms of sum/prod

**Usage**  
```
rxSumProdModel(model, expand = FALSE, sum = TRUE, prod = TRUE)
```

**Arguments**  
- `model`: RxODE model
- `expand`: Boolean indicating if the expression is expanded.
- `sum`: Use `sum(...)`
- `prod`: Use `prod(...)`

**Value**  
model string with prod(.) and sum(.) for all these operations.

**Author(s)**  
Matthew L. Fidler

---

**rxSymInvChol**  
*Get Omega^-1 and derivatives*

**Description**  
Get Omega^-1 and derivatives

**Usage**  
```
rxSymInvChol(invObjOrMatrix, theta = NULL, type = "cholOmegaInv",
             thetaNumber = 0L)
```
Arguments

invObjOrMatrix Object for inverse-type calculations. If this is a matrix, setup the object for inversion by \texttt{rxSymInvCholCreate} with the default arguments and return a reactive \texttt{s3} object. Otherwise, use the inversion object to calculate the requested derivative/inverse.

theta Thetas to be used for calculation. If missing (\texttt{NULL}), a special \texttt{s3} class is created and returned to access \texttt{Omega^1} objects as needed and cache them based on the theta that is used.

type The type of object. Currently the following types are supported:

- \texttt{cholOmegaInv} gives the Cholesky decomposition of the Omega Inverse matrix.
- \texttt{omegaInv} gives the Omega Inverse matrix.
- \texttt{d(omegaInv)} gives the \texttt{d(Omega^\cdot1)} with respect to the theta parameter specified in \texttt{thetaNumber}.
- \texttt{d(D)} gives the \texttt{d(diagonal(Omega^\cdot1))} with respect to the theta parameter specified in the \texttt{thetaNumber} parameter

thetaNumber For types \texttt{d(omegaInv)} and \texttt{d(D)}, the theta number that the derivative is taken against. This must be positive from 1 to the number of thetas defining the Omega matrix.

Value

Matrix based on parameters or environment with all the matrixes calculated in variables \texttt{omega}, \texttt{omegaInv}, \texttt{dOmega}, \texttt{dOmegaInv}.

Author(s)

Matthew L. Fidler

---

\texttt{rxSymPyFix} \hspace{3cm} \textit{Fix SymPy expressions to be R parsable expressions}

Description

Fix SymPy expressions to be R parsable expressions

Usage

\texttt{rxSymPyFix(var)}

Arguments

\texttt{var} \hspace{3cm} \texttt{sympy expression}
Value

R valid expression

Author(s)

Matthew L. Fidler

---

rxSymPySensitivity  
*Calculate the sensitivity equations for a model*

Description

This expands the model to calculate sensitivities. This requires rSymPy.

Usage

```r
rxSymPySensitivity(model, calcSens, calcJac = FALSE, keepState = NULL,
collapseModel = FALSE)
```

Arguments

- **model**: RxODE family of objects
- **calcSens**: Either a logical or list of sensitivity parameters to calculate. When TRUE, calculate the sensitivities of all the known parameters. When FALSE raise an error.
- **calcJac**: A boolean that determines if the Jacobian should be calculated.
- **keepState**: State parameters to keep the sensitivities for.
- **collapseModel**: A boolean to collapse the model that each expression only depends on the unspecified parameters (instead on LHS quantities).

Value

Model syntax that includes the sensitivity parameters.

Author(s)

Matthew L. Fidler
**rxSymPyVersion**

*Return the version of SymPy that is running*

**Description**

Return the version of SymPy that is running

**Usage**

```
rxSymPyVersion(numeric = TRUE)
```

**Arguments**

- **numeric**
  
  boolean that specifies if the major and minor release should be a number.

**Value**

Version of sympy that is running.

**Author(s)**

Matthew L. Fidler

---

**rxSyncOptions**

*Sync options with RxODE varaibles*

**Description**

Accessing RxODE options via getOption slows down solving. This allows the options to be synced with variables.

**Usage**

```
rxSyncOptions()
```

**Author(s)**

Matthew L. Fidler
Translate the model to C code if needed

Description

This function translates the model to C code, if needed

Usage

```c
rxTrans(model, cFile = sprintf("%s.c", gsub("\.[^.]\*$", "", model)),
        extraC = NULL, modelPrefix = "", md5 = "", modName = NULL,
        modVars = FALSE, calcSens = NULL, calcJac = NULL,
        collapseModel = FALSE, ...)
```

## Default S3 method:

```c
rxTrans(model, cFile = sprintf("%s.c",
        gsub("\.[^.]\*$", "", model)), extraC = NULL, modelPrefix = "",
        md5 = "", modName = NULL, modVars = FALSE, calcSens = NULL,
        calcJac = NULL, collapseModel = FALSE, ...)
```

## S3 method for class 'character'

```c
rxTrans(model, cFile = sprintf("%s.c",
        gsub("\.[^.]\*$", "", model)), extraC = NULL, modelPrefix = "",
        md5 = "", modName = NULL, modVars = FALSE, calcSens = NULL,
        calcJac = NULL, collapseModel = FALSE, ...)
```

Arguments

- `model` This is the ODE model specification. It can be:
  - a string containing the set of ordinary differential equations (ODE) and
    other expressions defining the changes in the dynamic system.
  - a file name where the ODE system equation is contained
  - An ODE expression enclosed in `{}`

(see also the `filename` argument). For details, see the sections “Details” and
“RxODE Syntax” below.

- `cFile` The C file where the code should be output

- `extraC` Extra C code to include in the model. This can be useful to specify functions in
  the model. These C functions should usually take double precision arguments,
  and return double precision values.

- `modelPrefix` Prefix of the model functions that will be compiled to make sure that multiple
  RxODE objects can coexist in the same R session.

- `md5` Is the md5 of the model before parsing, and is used to embed the md5 into DLL,
  and then provide for functions like `rxModelVars`. 
modName a string to be used as the model name. This string is used for naming various aspects of the computations, including generating C symbol names, dynamic libraries, etc. Therefore, it is necessary that modName consists of simple ASCII alphanumeric characters starting with a letter.

cmodVars returns the model variables instead of the named vector of translated properties.

calcSens boolean indicating if RxODE will calculate the sensitivities according to the specified ODEs.

calcJac boolean indicating if RxODE will calculate the Jacobian according to the specified ODEs.

collapseModel boolean indicating if RxODE will remove all LHS variables when calculating sensitivities.

... Ignored parameters.

Value

a named vector of translated model properties including what type of jacobian is specified, the C function prefixes, as well as the C functions names to be called through the compiled model.

Author(s)

Matthew L. Fidler

See Also

RxODE, rxCompile.

rxValidate Validate RxODE

Description

This allows easy validation/qualification of nlmixr by running the testing suite on your system.

Usage

rxValidate(full = TRUE)
rxTest(full = TRUE)

Arguments

full Should a full validation be performed? (By default TRUE)

Author(s)

Matthew L. Fidler
**rxWinPythonSetup**

*Setup Python and SymPy for windows*

**Description**

Setup Python and SymPy for windows

**Usage**

```
rxWinPythonSetup()
```

**Author(s)**

Matthew L. Fidler

---

**rxWinSetup**

*Setup Windows components for RxODE*

**Description**

Setup Windows components for RxODE

**Usage**

```
rxWinSetup(rm.rtools = TRUE, rm.python = TRUE)
```

**Arguments**

- `rm.rtools`: Remove the Rtools from the current path specs.
- `rm.python`: Remove Python from the current path specs.

**Author(s)**

Matthew L. Fidler
sqrtm

Return the square root of general square matrix A

Description

Return the square root of general square matrix A

Usage

sqrtm(m)

Arguments

m Matrix to take the square root of.

summary.RxODE Print expanded information about the RxODE object.

Description

This prints the expanded information about the RxODE object.

Usage

## S3 method for class 'RxODE'
summary(object, ...)

Arguments

object RxODE object
...
Ignored parameters

Author(s)

Matthew L.Fidler
**Description**

Yeo-Johnson Transformation

**Usage**

`yeoJohnson(x, lambda = 1)`

**Arguments**

- `x`: data to transform
- `lambda`: Cox-box lambda parameter

**Value**

Yeo-Johnson Transformed Data

**Author(s)**

Matthew L. Fidler
Index

*Topic **Internal**
  - print.rxCoefSolve, 15
*Topic **data**
  - eventTable, 11
*Topic **models**
  - eventTable, 11
  - RxODE, 26
*Topic **nonlinear**
  - genShinyApp.template, 13
  - RxODE, 26
*Topic **simulation**
  - genShinyApp.template, 13
  + .solveRxDll (rxChain), 18
  + .Call, 20
  + .rxRmPrint, 3
  + .rxRmSens, 4
  + .rxRtoolsBaseWin, 5
  + .rxSymPyJacobian, 5
  + .rxWinRtoolsPath, 6
  + add.dosing, 6
  + add.sampling, 7
  + cholSE, 8
  + coef.RxCompilationManager (coef.RxODE), 9
  + coef.rxDll (coef.RxODE), 9
  + coef.RxODE, 9
  + coef.solveRxODE (coef.RxODE), 9
  + coxBox, 10
  + cvPost, 10
  + eventTable, 7, 8, 11, 14, 27, 29, 39, 42
  + genShinyApp.template, 13
  + is.rxSolve, 15
  + predict.RxODE (rxSolve), 38
  + predict.rxSolve (rxSolve), 38
  + print.rxCoefSolve, 15
  + print.RxODE, 16
  + readLines, 27
  + rinvchisq, 16
  + rmvn, 37, 41
  + rmvt, 37, 41
  + rxAddReturn, 17
  + rxAssignPtr, 17
  + rxChain, 18
  + rxClean, 18
  + rxCompile, 19, 49
  + rxCores, 21, 40
  + rxDelete, 21
  + rxDfdy, 22
  + rxFoExpandEta, 22
  + rxGetRxODE, 23
  + rxHtml, 23
  + rxInv, 24
  + rxIsCurrent, 24
  + rxLhs, 25
  + rxModelVars, 48
  + rxNorm, 25
  + RxODE, 7, 8, 12, 14, 20, 25, 26, 43, 49
  + rxOptExpr, 30
  + rxOptions, 31
  + rxParam (rxParams), 32
  + rxParams, 32
  + rxPermissive, 33
  + rxProgress, 33
  + rxProgressAbort (rxProgress), 33
  + rxProgressStop (rxProgress), 33
  + rxSetProd, 34
  + rxSetSum, 35
  + rxShiny, 36
  + rxSimThetaOmega, 37
  + rxSolve, 14, 27, 38
  + rxSolveFree, 42
  + rxState, 43
  + rxStrict (rxPermissive), 33
rxSumProdModel, 44
rxSymInvChol, 44
rxSymInvCholCreate, 45
rxSymPyFix, 45
rxSymPySensitivity, 46
rxSymPyVersion, 47
rxSyncOptions, 47
rxTest (rxValidate), 49
rxTick (rxProgress), 33
rxTrans, 20, 48
rxValidate, 49
rxWinPythonSetup, 50
rxWinSetup, 50
simulate.RxODE (rxSolve), 38
simulate.rxSolve (rxSolve), 38
solve.RxODE (rxSolve), 38
solve.rxSolve (rxSolve), 38
sqrtm, 51
summary.RxODE, 51
update.rxSolve (rxSolve), 38
write.template.server
   (genShinyApp.template), 13
write.template.ui, 14
write.template.ui
   (genShinyApp.template), 13
yeoJohnson, 52