Package 'dMod'

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Type Package

Title Dynamic Modeling and Parameter Estimation in ODE Models

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Description The framework provides functions to generate ODEs of reaction networks, parameter transformations, observation functions, residual functions, etc. The framework follows the paradigm that derivative information should be used for optimization whenever possible. Therefore, all major functions produce and can handle expressions for symbolic derivatives. The methods used in dMod were published in Kaschek et al, 2019, <doi:10.18637/jss.v088.i10>.

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R topics documented:

`*.fn` *Concatenation of functions*

Description

Used to concatenate observation functions, prediction functions and parameter transformation functions.

Usage

```
## S3 method for class 'fn'
p1 * p2
```

Arguments

`p1`	function of class `obsfn`, `prdfn`, `parfn` or `idfn`
`p2`	function of class `obsfn`, `prdfn`, `parfn` or `idfn`

Value

Object of the same class as `x1` and `x2`.

Examples

```
# Define a time grid on which to make a prediction by peace-wise linear function.
# Then define a (generic) prediction function based on thid grid.
times <- 0:5
grid <- data.frame(name = "A", time = times, row.names = paste0("p", times))
x <- Xd(grid)

# Define an observable and an observation function
observables <- eqnvec(Aobs = "s*A")
g <- Y(g = observables, f = NULL, states = "A", parameters = "s")

# Collect parameters and define an overarching parameter transformation
# for two "experimental condtions".
dynpars <- attr(x, "parameters")
obspars <- attr(g, "parameters")
innerpars <- c(dynpars, obspars)

trafo <- structure(innerpars, names = innerpars)
trafo_C1 <- replaceSymbols(innerpars, paste(innerpars, "C1", sep = "_"), trafo)
trafo_C2 <- replaceSymbols(innerpars, paste(innerpars, "C2", sep = "_"), trafo)

p <- NULL
p <- p + P(trafo = trafo_C1, condition = "C1")
p <- p + P(trafo = trafo_C2, condition = "C2")

# Collect outer (overarching) parameters and
# initialize with random values
outerpars <- attr(p, "parameters")
pars <- structure(runif(length(outerpars), 0, 1), names = outerpars)

# Predict internal/unobserved states
out1 <- (x*p)(times, pars)
plot(out1)

# Predict observed states in addition to unobserved
out2 <- (g*x*p)(times, pars)
plot(out2)
```

+.datalist *Direct sum of datasets*

Description

Used to merge datasets with overlapping conditions.

Usage

```
## S3 method for class 'datalist'
data1 + data2
```

Arguments

data1	dataset of class datalist
data2	dataset of class datalist

Details

Each data list contains data frames for a number of conditions. The direct sum of datalist is meant as merging the two data lists and returning the overarching datalist.

Value

Object of class datalist for the union of conditions.

Examples

```
# Start with two data frames
mydata1 <- data.frame(
  name = "A",
  time = 0:1,
  value = 1:2,
  sigma = .1,
  compound = c("DEM", "APAP"),
  dose = "0.1"
)

mydata2 <- data.frame(
  name = "A",
  time = 0:1,
  value = 3:4,
  sigma = .1,
  compound = c("APAP", "DCF"),
  dose = "0.1"
)

# Create datalists from dataframes
data1 <- as.datalist(mydata1, split.by = c("compound", "dose"))
data2 <- as.datalist(mydata2, split.by = c("compound", "dose"))

# Direct sum of datalists
 data <- data1 + data2
 print(data)

# Check the condition.grid (if available)
 condition.grid <- attr(data, "condition.grid")
 print(condition.grid)
```

+.fn *Direct sum of functions*

Description

Used to add prediction function, parameter transformation functions or observation functions.

Usage

```
## S3 method for class 'fn'
x1 + x2
```

Arguments

x1	function of class obsfn, prdfn or parfn
x2	function of class obsfn, prdfn or parfn

Details

Each prediction function is associated to a number of conditions. Adding functions means merging or overwriting the set of conditions.

Value

Object of the same class as x1 and x2 which returns results for the union of conditions.

See Also

P, Y, Xs

Examples

```
# Define a time grid on which to make a prediction by peace-wise linear function.
# Then define a (generic) prediction function based on thid grid.
times <- 0:5
grid <- data.frame(name = "A", time = times, row.names = paste0("p", times))
x <- Xd(grid)

# Define an observable and an observation function
observables <- eqnvec(Aobs = "s*A")
g <- Y(g = observables, f = NULL, states = "A", parameters = "s")

# Collect parameters and define an overarching parameter transformation
# for two "experimental condtions".
dynpars <- attr(x, "parameters")
obspars <- attr(g, "parameters")
innerpars <- c(dynpars, obspars)

trafo <- structure(innerpars, names = innerpars)
```

```
trafo_C1 <- replaceSymbols(innerpars, paste(innerpars, "C1", sep = "_"), trafo)
trafo_C2 <- replaceSymbols(innerpars, paste(innerpars, "C2", sep = "_"), trafo)

p <- NULL
p <- p + P(trafo = trafo_C1, condition = "C1")
p <- p + P(trafo = trafo_C2, condition = "C2")

# Collect outer (overarching) parameters and
# initialize with random values
outerpars <- attr(p, "parameters")
pars <- structure(runif(length(outerpars), 0, 1), names = outerpars)

# Predict internal/unobserved states
out1 <- (x*p)(times, pars)
plot(out1)

# Predict observed states in addition to unobserved
out2 <- (g*x*p)(times, pars)
plot(out2)
```

`+.objfn` *Direct sum of objective functions*

Description

Direct sum of objective functions

Usage

```
## S3 method for class 'objfn'
x1 + x2
```

Arguments

`x1`	function of class `objfn`
`x2`	function of class `objfn`

Details

The objective functions are evaluated and their results as added. Sometimes, the evaluation of an objective function depends on results that have been computed internally in a preceding objective function. Therefore, environments are forwarded and all evaluations take place in the same environment. The first objective function in a sum of functions generates a new environment.

Value

Object of class `objfn`.

See Also

normL2, constraintL2, priorL2, datapointL2

Examples

```
## Generate three objective functions
prior <- structure(rep(0, 5), names = letters[1:5])

obj1 <- constraintL2(mu = prior, attr.name = "center")
obj2 <- constraintL2(mu = prior + 1, attr.name = "right")
obj3 <- constraintL2(mu = prior - 1, attr.name = "left")

## Evaluate first objective function on a random vector
pouter <- prior + rnorm(length(prior))
print(obj1(pouter))

## Split into fixed and non-fixed part
fixed <- pouter[4:5]
pouter <- pouter[1:3]
print(obj1(pouter, fixed = fixed))


## Visualize the result by a parameter profile
myfit <- trust(obj1, pouter, rinit = 1, rmax = 10, fixed = fixed)
myprof <- profile(obj1, myfit$argument, "a", fixed = fixed)
plotProfile(myprof)


## Create new objective function by adding the single ones,
## then evalue the random vector again
pouter <- prior + rnorm(length(prior))
obj <- obj1 + obj2 + obj3
print(obj(pouter))
```

+.objlist *Add two lists element by element*

Description

Add two lists element by element

Usage

```
## S3 method for class 'objlist'
out1 + out2
```

Arguments

out1	List of numerics or matrices
out2	List with the same structure as out1 (there will be no warning when mismatching)

Details

If out1 has names, out2 is assumed to share these names. Each element of the list out1 is inspected. If it has a names attributed, it is used to do a matching between out1 and out2. The same holds for the attributed dimnames. In all other cases, the "+" operator is applied the corresponding elements of out1 and out2 as they are.

Value

List of length of out1.

---

addReaction *Add reaction to reaction table*

Description

Add reaction to reaction table

Usage

```
addReaction(eqnlist, from, to, rate, description = names(rate))
```

Arguments

eqnlist	equation list, see eqnlist
from	character with the left hand side of the reaction, e.g. "2*A + B"
to	character with the right hand side of the reaction, e.g. "C + 2*D"
rate	character. The rate associated with the reaction. The name is employed as a description of the reaction.
description	Optional description instead of names(rate).

Value

An object of class eqnlist.

Examples

```
f <- eqnlist()
f <- addReaction(f, "2*A+B", "C + 2*D", "k1*B*A^2")
f <- addReaction(f, "C + A", "B + A", "k2*C*A")



  # Write your example here. You can also add more Start..End blocks if needed.
  # Please mask all output such as print() with the special tag
  #
  # such that the test is not littered. Statements guarded by  are enabled
  # in the example file which is extracted from this test file. To extract the
  # example run
  #    extractExamples()
  # on the R command line.

    ## Generate another equation list
    eq <- eqnlist()
    eq <- addReaction(eq, "A", "pA", "act_A * A * stimulus", "Phosphorylation of A")
    eq <- addReaction(eq, "pA", "A", "deact_A * pA", "Deposphorylation of pA")
   eq <- addReaction(eq, "2*pA", "pA_pA", "form_complex_pA * pA^2", "Complex formation of pA")
    eq <- addReaction(eq, "B", "pB", "act_B * B * pA_pA", "Phosphorylation of B")
    eq <- addReaction(eq, "pB", "B", "deact_B * pB", "Deposphorylation of pB")

    ## Extract data.frame of reactions
    reactions <- getReactions(eq)
     print(reactions)

    ## Get conserved quantities
    cq <- conservedQuantities(eq$smatrix)
     print(cq)

    ## Get fluxes
    fluxes <- getFluxes(eq)
     print(fluxes)

    ## Subsetting of equation list
    subeq1 <- subset(eq, "pB" %in% Product)
     print(subeq1)
    subeq2 <- subset(eq, grepl("not_available", Description))
     print(subeq2)

    ## Time derivatives of observables
    observables <- eqnvec(pA_obs = "s1*pA", tA_obs = "s2*(A + pA)")
    dobs <- dot(observables, eq)

    ## Combined equation vector for ODE and observables
    f <- c(as.eqnvec(eq), dobs)
     print(f)
```

as.data.frame.datalist *Coerce to a Data Frame*

Description

Coerce to a Data Frame

Usage

```
## S3 method for class 'datalist'
as.data.frame(x, ...)

## S3 method for class 'prdlist'
as.data.frame(x, ..., data = NULL, errfn = NULL)
```

Arguments

x	any R object
...	not used right now
data	data list oject
errfn	obsfn object, the error model function to predict sigma

Value

a data frame

as.data.frame.eqnlist *Coerce equation list into a data frame*

Description

Coerce equation list into a data frame

Usage

```
## S3 method for class 'eqnlist'
as.data.frame(x, ...)
```

Arguments

x	object of class eqnlist
...	other arguments

Value

a `data.frame` with columns "Description" (character), "Rate" (character), and one column per ODE state with the state names. The state columns correspond to the stoichiometric matrix.

`as.eqnvec` *Coerce to an equation vector*

Description

An equation list stores an ODE in a list format. The function translates this list into the right-hand sides of the ODE.

Usage

```
as.eqnvec(x, ...)

## S3 method for class 'character'
as.eqnvec(x = NULL, names = NULL, ...)

## S3 method for class 'eqnlist'
as.eqnvec(x, ...)
```

Arguments

`x`	object of class `character` or `eqnlist`
`...`	arguments going to the corresponding methods
`names`	character, the left-hand sides of the equation

Details

If `x` is of class `eqnlist`, getFluxes is called and coerced into a vector of equations.

Value

object of class eqnvec.

as.eventlist *Coerce to eventlist*

Description

Coerce to eventlist

Usage

```
as.eventlist(x, ...)

## S3 method for class 'list'
as.eventlist(x, ...)

## S3 method for class 'data.frame'
as.eventlist(x, ...)
```

Arguments

x	list, data.frame
...	not used

as.objlist *Generate objective list from numeric vector*

Description

Generate objective list from numeric vector

Usage

```
as.objlist(p)
```

Arguments

p	Named numeric vector

Value

list with entries value (`0`), gradient (`rep(0, length(p))`) and hessian (`matrix(0, length(p), length(p))`) of class `obj`.

Examples

```
p <- c(A = 1, B = 2)
as.objlist(p)
```

`as.parframe.parlist` *Coerce object to a parameter frame*

Description

Coerce object to a parameter frame

Usage

```
## S3 method for class 'parlist'
as.parframe(x, sort.by = "value", ...)

as.parframe(x, ...)
```

Arguments

`x`	object to be coerced
`sort.by`	character indicating by which colum the returned parameter frame should be sorted. Defaults to `"value"`.
`...`	other arguments

Value

object of class parframe.

Examples

```
## Generate a prediction function
regfn <- c(y = "sin(a*time)")

g <- Y(regfn, parameters = "a")
x <- Xt(condition = "C1")

## Generate data
data <- datalist(
  C1 = data.frame(
    name = "y",
    time = 1:5,
    value = sin(1:5) + rnorm(5, 0, .1),
    sigma = .1
  )
)

## Initialize parameters and time
pars <- c(a = 1)
times <- seq(0, 5, .1)

plot((g*x)(times, pars), data)
```

```
## Do many fits from random positions and store them into parlist
out <- as.parlist(lapply(1:50, function(i) {
  trust(normL2(data, g*x), pars + rnorm(length(pars), 0, 1), rinit = 1, rmax = 10)
}))

summary(out)

## Reduce parlist to parframe
parframe <- as.parframe(out)
plotValues(parframe)

## Reduce parframe to best fit
bestfit <- as.parvec(parframe)
plot((g*x)(times, bestfit), data)
```

`as.parvec.parframe` *Select a parameter vector from a parameter frame.*

Description

Obtain a parameter vector from a parameter frame.

Usage

```
## S3 method for class 'parframe'
as.parvec(x, index = 1, ...)
```

Arguments

`x`	A parameter frame, e.g., the output of `as.parframe`.
`index`	Integer, the parameter vector with the `index`-th lowest objective value.
`...`	not used right now

Details

With this command, additional information included in the parameter frame as the objective value and the convergence state are removed and a parameter vector is returned. This parameter vector can be used to e.g., evaluate an objective function.

On selection, the parameters in the parameter frame are ordered such, that the parameter vector with the lowest objective value is at '`index`' 1. Thus, the parameter vector with the '`index`'-th lowest objective value is easily obtained.

Value

The parameter vector with the '`index`'-th lowest objective value.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

`attrs` *Select attributes.*

Description

Select or discard attributes from an object.

Usage

```
attrs(x, atr = NULL, keep = TRUE)
```

Arguments

`x`	The object to work on
`atr`	An optional list of attributes which are either kept or removed. This parameter defaults to dim, dimnames, names, col.names, and row.names.
`keep`	For keep = TRUE, atr is a positive list on attributes which are kept, for keep = FALSE, 'atr' are removed.

Value

x with selected attributes.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

Mirjam Fehling-Kaschek, <mirjam.fehling@physik.uni-freiburg.de>

`blockdiagSymb` *Embed two matrices into one blockdiagonal matrix*

Description

Embed two matrices into one blockdiagonal matrix

Usage

```
blockdiagSymb(M, N)
```

Arguments

`M`	matrix of type character
`N`	matrix of type character

Value

Matrix of type character containing M and N as upper left and lower right block

Examples

```
M <- matrix(1:9, 3, 3, dimnames = list(letters[1:3], letters[1:3]))
N <- matrix(1:4, 2, 2, dimnames = list(LETTERS[1:2], LETTERS[1:2]))
blockdiagSymb(M, N)
```

---

combine *Combine several data.frames by rowbind*

Description

Combine several data.frames by rowbind

Usage

```
combine(...)
```

Arguments

...	data.frames or matrices with not necessarily overlapping colnames

Details

This function is useful when separating models into independent csv model files, e.g.~a receptor model and several downstream pathways. Then, the models can be recombined into one model by `combine()`.

Value

A `data.frame`

Examples

```
data1 <- data.frame(Description = "reaction 1", Rate = "k1*A", A = -1, B = 1)
data2 <- data.frame(Description = "reaction 2", Rate = "k2*B", B = -1, C = 1)
combine(data1, data2)
```

compare *Compare two objects and return differences*

Description

Works eigher on a list or on two arguments. In case of a list, comparison is done with respect to a reference entry. Besides the objects themselves also some of their attributes are compared, i.e. "equations", "parameters" and "events" and "forcings".

Usage

```
compare(vec1, ...)

## S3 method for class 'list'
compare(vec1, vec2 = NULL, reference = 1, ...)

## S3 method for class 'character'
compare(vec1, vec2 = NULL, ...)

## S3 method for class 'eqnvec'
compare(vec1, vec2 = NULL, ...)

## S3 method for class 'data.frame'
compare(vec1, vec2 = NULL, ...)
```

Arguments

vec1	object of class eqnvec, character or data.frame. Alternatively, a list of such objects.
...	arguments going to the corresponding methods
vec2	same as vec1. Not used if vec1 is a list.
reference	numeric of length one, the reference entry.

Value

data.frame or list of data.frames with the differences.

Examples

```
## Compare equation vectors
eq1 <- eqnvec(a = "-k1*a + k2*b", b = "k2*a - k2*b")
eq2 <- eqnvec(a = "-k1*a", b = "k2*a - k2*b", c = "k2*b")
compare(eq1, eq2)

## Compare character vectors
c1 <- c("a", "b")
c2 <- c("b", "c")
```

```
compare(c1, c2)

## Compare data.frames
d1 <- data.frame(var = "a", time = 1, value = 1:3, method = "replace")
d2 <- data.frame(var = "a", time = 1, value = 2:4, method = "replace")
compare(d1, d2)

## Compare structures like prediction functions
fn1 <- function(x) x^2
attr(fn1, "equations") <- eq1
attr(fn1, "parameters") <- c1
attr(fn1, "events") <- d1

fn2 <- function(x) x^3
attr(fn2, "equations") <- eq2
attr(fn2, "parameters") <- c2
attr(fn2, "events") <- d2

mylist <- list(f1 = fn1, f2 = fn2)
compare(mylist)
```

`compile` *Compile one or more prdfn, obsfn or parfn objects*

Description

Compile one or more prdfn, obsfn or parfn objects

Usage

```
compile(..., output = NULL, args = NULL, cores = 1, verbose = F)
```

Arguments

`...`	Objects of class parfn, obsfn or prdfn
`output`	Optional character of the file to be produced. If several objects were passed, the different C files are all compiled into one shared object file.
`args`	Additional arguments for the R CMD SHLIB call, e.g. `-leinspline`.
`cores`	Number of cores used for compilation when several files are compiled.
`verbose`	Print compiler output to R command line.

confint.parframe *Profile uncertainty extraction*

Description

extract parameter uncertainties from profiles

Usage

```
## S3 method for class 'parframe'
confint(object, parm = NULL, level = 0.95, ..., val.column = "data")
```

Arguments

object	object of class parframe, returned from profile function.
parm	a specification of which parameters are to be given confidence intervals, either a vector of numbers or a vector of names. If missing, all parameters are considered.
level	the confidence level required.
...	not used right now.
val.column	the value column used in the parframe, usually 'data'.

conservedQuantities *Determine conserved quantites by finding the kernel of the stoichiometric matrix*

Description

Determine conserved quantites by finding the kernel of the stoichiometric matrix

Usage

```
conservedQuantities(S)
```

Arguments

S	Stoichiometric matrix

Value

Data frame with conserved quantities carrying an attribute with the number of conserved quantities.

Author(s)

Malenke Mader, <Malenka.Mader@fdm.uni-freiburg.de>

Examples

```
# Write your example here. You can also add more Start..End blocks if needed.
# Please mask all output such as print() with the special tag
#
# such that the test is not littered. Statements guarded by  are enabled
# in the example file which is extracted from this test file. To extract the
# example run
#    extractExamples()
# on the R command line.

  ## Generate another equation list
  eq <- eqnlist()
  eq <- addReaction(eq, "A", "pA", "act_A * A * stimulus", "Phosphorylation of A")
  eq <- addReaction(eq, "pA", "A", "deact_A * pA", "Deposphorylation of pA")
 eq <- addReaction(eq, "2*pA", "pA_pA", "form_complex_pA * pA^2", "Complex formation of pA")
  eq <- addReaction(eq, "B", "pB", "act_B * B * pA_pA", "Phosphorylation of B")
  eq <- addReaction(eq, "pB", "B", "deact_B * pB", "Deposphorylation of pB")

  ## Extract data.frame of reactions
  reactions <- getReactions(eq)
   print(reactions)

  ## Get conserved quantities
  cq <- conservedQuantities(eq$smatrix)
   print(cq)

  ## Get fluxes
  fluxes <- getFluxes(eq)
   print(fluxes)

  ## Subsetting of equation list
  subeq1 <- subset(eq, "pB" %in% Product)
   print(subeq1)
  subeq2 <- subset(eq, grepl("not_available", Description))
   print(subeq2)

  ## Time derivatives of observables
  observables <- eqnvec(pA_obs = "s1*pA", tA_obs = "s2*(A + pA)")
  dobs <- dot(observables, eq)

  ## Combined equation vector for ODE and observables
  f <- c(as.eqnvec(eq), dobs)
   print(f)
```

---

constraintExp2 *Compute a differentiable box prior*

Description

Compute a differentiable box prior

Usage

```
constraintExp2(p, mu, sigma = 1, k = 0.05, fixed = NULL)
```

Arguments

p	Named numeric, the parameter value
mu	Named numeric, the prior values, means of boxes
sigma	Named numeric, half box width
k	Named numeric, shape of box; if 0 a quadratic prior is obtained, the higher k the more box shape, gradient at border of the box (-sigma, sigma) is equal to sigma*k
fixed	Named numeric with fixed parameter values (contribute to the prior value but not to gradient and Hessian)

Value

list with entries: value (numeric, the weighted residual sum of squares), gradient (numeric, gradient) and hessian (matrix of type numeric). Object of class `objlist`.

---

constraintL2 *Soft L2 constraint on parameters*

Description

Soft L2 constraint on parameters

Usage

```
constraintL2(mu, sigma = 1, attr.name = "prior", condition = NULL)
```

Arguments

mu	named numeric, the prior values
sigma	named numeric of length of mu or numeric of length one or character of length of mu or character of length one
attr.name	character. The constraint value is additionally returned in an attributed with this name
condition	character, the condition for which the constraint should apply. If `NULL`, applies to any condition.

Details

If sigma is numeric, the function computes the constraint value

$$\left(\frac{p-\mu}{\sigma}\right)^2$$

and its derivatives with respect to p. If sigma is a character, the function computes

$$\left(\frac{p-\mu}{\sigma}\right)^2 + \log(\sigma^2)$$

and its derivatives with respect to p and sigma. Sigma parameters being passed to the function are ALWAYS assumed to be on a log scale, i.e. internally sigma parameters are converted by `exp()`.

Value

object of class `objfn`

See Also

wrss

Examples

```
mu <- c(A = 0, B = 0)
sigma <- c(A = 0.1, B = 1)
myfn <- constraintL2(mu, sigma)
myfn(pars = c(A = 1, B = -1))

# Introduce sigma parameter but fix them (sigma parameters
# are assumed to be passed on log scale)
mu <- c(A = 0, B = 0)
sigma <- paste("sigma", names(mu), sep = "_")
myfn <- constraintL2(mu, sigma)
pars <- c(A = .8, B = -.3, sigma_A = -1, sigma_B = 1)
myfn(pars = pars[c(1, 3)], fixed = pars[c(2, 4)])

# Assume same sigma parameter for both A and B
# sigma is assumed to be passed on log scale
mu <- c(A = 0, B = 0)
myfn <- constraintL2(mu, sigma = "sigma")
pars <- c(A = .8, B = -.3, sigma = 0)
myfn(pars = pars)
```

controls *List, get and set controls for different functions*

Description

Applies to objects of class `objfn`, `parfn`, `prdfn` and `obsfn`. Allows to manipulate different arguments that have been set when creating the objects.

Usage

```
controls(x, ...)

## S3 method for class 'objfn'
controls(x, name = NULL, ...)

## S3 method for class 'fn'
controls(x, condition = NULL, name = NULL, ...)

controls(x, ...) <- value

## S3 replacement method for class 'objfn'
controls(x, name, ...) <- value

## S3 replacement method for class 'fn'
controls(x, condition = NULL, name, ...) <- value
```

Arguments

`x`	function
`...`	arguments going to the appropriate S3 methods
`name`	character, the name of the control
`condition`	character, the condition name
`value`	the new value

Details

If called without further arguments, `controls(x)` lists the available controls within an object. Calling `controls()` with `name` and `condition` returns the control value. The value can be overwritten. If a list or data.frame ist returned, elements of those can be manipulated by the `$`- or `[]`-operator.

Value

Either a print-out or the values of the control.

Examples

```
## parfn with condition
p <- P(eqnvec(x = "-a*x"), method = "implicit", condition = "C1")
controls(p)
controls(p, "C1", "keep.root")
controls(p, "C1", "keep.root") <- FALSE

## obsfn with NULL condition
g <- Y(g = eqnvec(y = "s*x"), f = NULL, states = "x", parameters = "s")
controls(g)
controls(g, NULL, "attach.input")
controls(g, NULL, "attach.input") <- FALSE
```

`coordTransform` *Coordinate transformation for data frames*

Description

Applies a symbolically defined transformation to the `value` column of a data frame. Additionally, if a `sigma` column is present, those values are transformed according to Gaussian error propagation.

Usage

```
coordTransform(data, transformations)
```

Arguments

`data`	data frame with at least columns "name" (character) and "value" (numeric). Can optionally contain a column "sigma" (numeric).
`transformations`	character (the transformation) or named list of characters. In this case, the list names must be a subset of those contained in the "name" column.

Value

The data frame with the transformed values and sigma uncertainties.

Examples

```
mydata1 <- data.frame(name = c("A", "B"), time = 0:5, value = 0:5, sigma = .1)
coordTransform(mydata1, "log(value)")
coordTransform(mydata1, list(A = "exp(value)", B = "sqrt(value)"))
```

covariates *Access the covariates in the data*

Description

Access the covariates in the data

Usage

```
covariates(x)

## S3 method for class 'datalist'
covariates(x)

## S3 method for class 'data.frame'
covariates(x)
```

Arguments

x	Either a datalist or a `data.frame` with mandatory columns `c("name", "time", "value", "sigma", "lloq")`.

Value

The `condition.grid` of the data

datalist *Generate a datalist object*

Description

The datalist object stores time-course data in a list of data.frames. The names of the list serve as identifiers, e.g. of an experimental condition, etc.

Usage

```
datalist(...)

as.datalist(x, ...)

## S3 method for class 'data.frame'
as.datalist(x, split.by = NULL, keep.covariates = NULL, ...)

## S3 method for class 'list'
as.datalist(x, names = NULL, ..., condition.grid = attr(x, "condition.grid"))
```

```
## S3 replacement method for class 'datalist'
names(x) <- value

is.datalist(x)

## S3 method for class 'datalist'
c(...)
```

Arguments

`...`	data.frame objects to be coerced into a list and additional arguments
`x`	object of class `data.frame` or `list`. Data frames are required to provide "name", "time" and "value" as columns. Columns "sigma" and "lloq" can be provided. If "sigma" and "lloq" are missing, they are imputed with `NA` and `-Inf`, respectively.
`split.by`	vector of columns names which yield a unique identifier (conditions). If NULL, all columns except for the expected standard columns "name", "time", "value", "sigma" and "lloq" will be selected.
`keep.covariates`	vector of additional column names which should be kept in the condition.grid.
`names`	optional names vector, otherwise names are taken from `mylist`
`condition.grid`	Optionally, to manually specify a condition.grid
`value`	The new condition names of the datalist and its condition.grid

Details

Datalists can be plotted, see plotData and merged, see sumdatalist. They are the basic structure when combining model prediction and data via the normL2 objective function.

The standard columns of the datalist data frames are "name" (observable name), "time" (time points), "value" (data value), "sigma" (uncertainty, can be NA), and "lloq" (lower limit of quantification, `-Inf` by default).

Datalists carry the attribute `condition.grid` which contains additional information about different conditions, such as dosing information for the experiment. It can be conveniently accessed by the covariates-function. Reassigning names to a datalist also renames the rows of the `condition.grid`.

Value

Object of class `datalist`.

Object of class datalist

Examples

```
## Generate datalist from scratch
mydata1 <- data.frame(name = "A",
                      time = 0:5,
                      value = 0:5,
                      sigma = .1,
                      lloq = -0.5)
```

```
mydata2 <- data.frame(name = "A",
                      time = 0:5,
                      value = sin(0:5),
                      sigma = .1)

data <- datalist(C1 = mydata1, C2 = mydata2)
print(data)
plot(data)

## Generate datalist from singla data.frame
times <- seq(0, 2*pi, length.out = 20)
mydata <- data.frame(name = "A",
                     time = times,
                     value = c(sin(times), 1.5 * sin(times)),
                     sigma = .1,
                     stage = rep(c("upper", "lower"), each = 10),
                     phase = rep(c("first", "second"), each = 20),
                     amplitude = rep(c(1,1.5), each = 20))

data <- as.datalist(mydata, split.by = c("stage", "phase"), keep.covariates = "amplitude")
print(data)
plot(data)

condition.grid <- attr(data, "condition.grid")
print(condition.grid)
```

`datapointL2` *L2 objective function for validation data point*

Description

L2 objective function for validation data point

Usage

```
datapointL2(name, time, value, sigma = 1, attr.name = "validation", condition)
```

Arguments

`name`	character, the name of the prediction, e.g. a state name.
`time`	numeric, the time-point associated to the prediction
`value`	character, the name of the parameter which contains the prediction value.
`sigma`	numeric, the uncertainty of the introduced test data point
`attr.name`	character. The constraint value is additionally returned in an attributed with this name
`condition`	character, the condition for which the prediction is made.

Details

Computes the constraint value

$$\left(\frac{x(t)-\mu}{\sigma}\right)^2$$

and its derivatives with respect to p.

Value

List of class `objlist`, i.e. objective value, gradient and Hessian as list.

See Also

wrss, constraintL2

Examples

```
prediction <- list(a = matrix(c(0, 1), nrow = 1, dimnames = list(NULL, c("time", "A"))))
derivs <- matrix(c(0, 1, 0.1), nrow = 1, dimnames = list(NULL, c("time", "A.A", "A.k1")))
attr(prediction$a, "deriv") <- derivs
p0 <- c(A = 1, k1 = 2)

vali <- datapointL2(name = "A", time = 0, value = "newpoint", sigma = 1, condition = "a")
vali(pars = c(p0, newpoint = 1), env = .GlobalEnv)
```

---

define *Define parameter transformations by* `define()`, `branch()` *and* `insert()`

Description

Define parameter transformations by `define()`, `branch()` and `insert()`

Usage

```
define(trafo, expr, ..., conditionMatch = NULL)

insert(trafo, expr, ..., conditionMatch = NULL)

branch(trafo, table = NULL, conditions = rownames(table))
```

Arguments

`trafo`	named character vector of parametric expressions or object of class `eqnvec`
`expr`	character of the form `"lhs ~ rhs"` where both `lhs` and `rhs` can contain a number of symbols for which vaues are passed by the `...` argument
`...`	used to pass values for symbols as named arguments

conditionMatch	optional character, Use as regular expression to apply the reparameterization only to conditions containing conditionMatch
table	table of covariates as data frame. Rownames are used as unique identifier, usually called "conditions", and columns represent covariates associated with these conditions.
conditions	character vector with condition names. Overwrites the rownames of table.

Value

object of the same class as trafo or list thereof, if `branch()` has been used.

Examples

```
# Define some parameter names
parameters <- c("A", "B", "k1", "k2")
# Define a covariate table
covtable <- data.frame(dose = c(1, 1, 10),
                       inhibitor = c("no", "inh", "no"),
                       row.names = c("Low_noInh", "Low_Inh", "High_noInh"))

# Start with an empty transformation
trans <- NULL

# Generate the identity transformation for parameters
trans <- define(trans, "x ~ x", x = parameters); print(trans)

# Insert exp(x) wherever you find x
trans <- insert(trans, "x ~ exp(x)", x = parameters); print(trans)

# Some new expressions instead of k1 and k2
trans <- insert(trans, "x ~ y", x = c("k1", "k2"), y = c("q1 + q2", "q1 - q2")); print(trans)

# Define some parameters as 0
trans <- define(trans, "x ~ 0", x = "B"); print(trans)

# The parameter name can also be directly used in the formula
trans <- insert(trans, "q1 ~ Q"); print(trans)

# Replicate the transformation 3 times with the rownames of covtable as list names
trans <- branch(trans, table = covtable); print(trans)

# Insert the rhs wherever the lhs is found in the transformation
# column names of covtable can be used to perform specific replacements
# for each transformation
trans <- insert(trans, "x ~ x_inh", x = c("Q", "q2"), inh = inhibitor); print(trans)

# Also numbers can be inserted
trans <- define(trans, "A ~ dose", dose = dose); print(trans)


# Turn that into a parameter transformation function
p <- P(trans)
```

```
parnames <- getParameters(p)
pars <- rnorm(length(parnames))
names(pars) <- parnames

p(pars)


# Advanced tricks exploiting the quoting-mechanism when capturing "..."

mydataframe <- data.frame(
  name = rep(letters[1:2], each = 3),
  value = 1:6,
  time = rep(1:3, 2),
  sigma = 0.1,
  par1 = rep(0:1, each = 3),
  par2 = rep(9:10, each = 3),
  par3 = rep(1:3, each = 2),
  stringsAsFactors = FALSE
)

parameters <- c("a", "b", "par1", "par2", "par3")
pars_to_insert <- c("par1", "par2")

# this would be the usual way when setting up a model
# pars_to_insert <- intersect(getParameters(g*x), names(data))

trafo <- define(NULL, "x~x", x = parameters)
trafo <- branch(trafo, covariates(as.datalist(mydataframe)))

# Trick 1: Access values from covariates()-Table with get/mget.
    # The names of the parameters which are supplied in the covariates()-table
    # have to be supplied manually.
trafo <- insert(trafo, "name ~ value", value = unlist(mget(pars_to_insert)), name = pars_to_insert)

# Trick 2: Access symbols from current condition-specific trafo with .currentSymbols, access
    # current condition-specific trafo by .currentTrafo
   # The input passed by the dots is "quoted" (substituted) and eval()'ed in the environment
    # of the lapply(1:length(conditions), function(i) {})
trafo <- insert(trafo, "x~exp(X)", x = .currentSymbols, X = toupper(.currentSymbols))

# Trick 3: Condition specificity. There are two ways to do this
 # 1. Apply reparametrization only for specific conditions using Regular Expressions for the
  # conditionMatch argument. This matches the condition name agains a regex
trafo <- define(NULL, "x~x", x = parameters)
trafo <- branch(trafo, covariates(as.datalist(mydataframe)))

# Conditions starting with 0_9
insert(trafo, "x~x_par3", x = "a", conditionMatch = "^0_9", par3 = par3)
# Conditions NOT starting with 0_9
insert(trafo, "x~0", x = "a", conditionMatch = "^(?!0_9)")
  # 2. Specify conditions by boolean arguments
  #    Conditions which satisfy par1 == 0
insert(trafo, "x~x_par2", par1 == 0, x = parameters, par2 = par2)
```

```
 # Special case: Pass two arguments with the same name. This is only possible if one of them
 # is logical and the other is not.
 # Conditions which satisfy par2 == 9
insert(trafo, "x~x_par2", par2 == 9, x = .currentSymbols, par2 = par2)
```

---

dot *Symbolic time derivative of equation vector given an equation list*

Description

The time evolution of the internal states is defined in the equation list. Time derivatives of observation functions are expressed in terms of the rates of the internal states.

Usage

```
dot(observable, eqnlist)
```

Arguments

observable	named character vector or object of type eqnvec
eqnlist	equation list

Details

Observables are translated into an ODE

Value

An object of class eqnvec

Examples

```
# Write your example here. You can also add more Start..End blocks if needed.
# Please mask all output such as print() with the special tag
#
# such that the test is not littered. Statements guarded by  are enabled
# in the example file which is extracted from this test file. To extract the
# example run
#    extractExamples()
# on the R command line.

  ## Generate another equation list
  eq <- eqnlist()
```

```
  eq <- addReaction(eq, "A", "pA", "act_A * A * stimulus", "Phosphorylation of A")
  eq <- addReaction(eq, "pA", "A", "deact_A * pA", "Deposphorylation of pA")
 eq <- addReaction(eq, "2*pA", "pA_pA", "form_complex_pA * pA^2", "Complex formation of pA")
  eq <- addReaction(eq, "B", "pB", "act_B * B * pA_pA", "Phosphorylation of B")
  eq <- addReaction(eq, "pB", "B", "deact_B * pB", "Deposphorylation of pB")

  ## Extract data.frame of reactions
  reactions <- getReactions(eq)
   print(reactions)

  ## Get conserved quantities
  cq <- conservedQuantities(eq$smatrix)
   print(cq)

  ## Get fluxes
  fluxes <- getFluxes(eq)
   print(fluxes)

  ## Subsetting of equation list
  subeq1 <- subset(eq, "pB" %in% Product)
   print(subeq1)
  subeq2 <- subset(eq, grepl("not_available", Description))
   print(subeq2)

  ## Time derivatives of observables
  observables <- eqnvec(pA_obs = "s1*pA", tA_obs = "s2*(A + pA)")
  dobs <- dot(observables, eq)

  ## Combined equation vector for ODE and observables
  f <- c(as.eqnvec(eq), dobs)
   print(f)
```

`eqnlist` *Generate eqnlist object*

Description

The eqnlist object stores an ODE as a list of stoichiometric matrix, rate expressions, state names and compartment volumes.

Translates a reaction network, e.g. defined by a data.frame, into an equation list object.

Usage

```
eqnlist(
  smatrix = NULL,
  states = colnames(smatrix),
```

```
  rates = NULL,
  volumes = NULL,
  description = NULL
)

as.eqnlist(data, volumes)

## S3 method for class 'data.frame'
as.eqnlist(data, volumes = NULL)

is.eqnlist(x)
```

Arguments

smatrix	Matrix of class numeric. The stoichiometric matrix, one row per reaction/process and one column per state.
states	Character vector. Names of the states.
rates	Character vector. The rate expressions.
volumes	Named character, volume parameters for states. Names must be a subset of the states. Values can be either characters, e.g. "V1", or numeric values for the volume. If volumes is not NULL, missing entries are treated as 1.
description	Character vector. Description of the single processes.
data	data.frame with columns Description, Rate, and one colum for each state reflecting the stoichiometric matrix
x	object of class eqnlist

Details

If data is a data.frame, it must contain columns "Description" (character), "Rate" (character), and one column per ODE state with the state names. The state columns correspond to the stoichiometric matrix.

Value

An object of class eqnlist, basically a list.

Object of class eqnlist

Examples

```
# Generate eqnlist from the constructor
S <- matrix(c(-1, 1, 1, -1),
            nrow = 2, ncol = 2,
            dimnames = list(NULL, c("A", "B")))

rates <- c("k1*A", "k2*B")
description <- c("forward", "backward")

f <- eqnlist(smatrix = S, rates = rates, description = description)
```

```
print(f)

# Convert to data.frame
fdata <- as.data.frame(f)
print(fdata)

# Generate eqnlist from data.frame and add volume parameter
f <- as.eqnlist(fdata, volumes = c(A = "Vcyt", B = "Vnuc"))
print(f)
print(as.eqnvec(f))
print(as.eqnvec(f, type = "amount"))
```

---

eqnvec *Generate equation vector object*

Description

The eqnvec object stores explicit algebraic equations, like the right-hand sides of an ODE, observation functions or parameter transformations as named character vectors.

Usage

```
eqnvec(...)

is.eqnvec(x)
```

Arguments

...	mathematical expressions as characters to be coerced, the right-hand sides of the equations
x	obect of any class

Value

object of class eqnvec, basically a named character.

See Also

eqnlist

Examples

```
v <- eqnvec(y = "2*x + offset")
print(v)
is.eqnvec(v)
```

`eventlist` *Eventlist*

Description

An eventlist is a data.frame with the necessary parameters to define an event as columns and specific events as rows. Event time and value can be passed as parameters, which can also be estimated.

Usage

```
eventlist(var = NULL, time = NULL, value = NULL, method = NULL)

addEvent(event, var, time = 0, value = 0, method = "replace", ...)
```

Arguments

`var`	Character, the state to which the event is applied
`time`	Character or Numeric, the time at which the event happens
`value`	Character or Numeric, the value of the event
`method`	Character, options are "replace", "add" or "multiply"
`event`	object of class `eventlist`
`...`	not used

Details

The function `addEvent` is pipe-friendly

Value

data.frame with class eventlist

Examples

```
eventlist(var = "A", time = "5", value = 1, method = "add")

events <- addEvent(NULL, var = "A", time = "5", value = 1, method = "add")
events <- addEvent(events, var = "A", time = "10", value = 1, method = "add")
```

expand.grid.alt *Alternative version of expand.grid*

Description

Alternative version of expand.grid

Usage

```
expand.grid.alt(seq1, seq2)
```

Arguments

seq1	Vector, numeric or character
seq2	Vector, numeric or character

Value

Matrix ob combinations of elemens of seq1 and seq2

fitErrorModel *Fit an error model*

Description

Fit an error model to reduced replicate data, see reduceReplicates.

Usage

```
fitErrorModel(
  data,
  factors,
  errorModel = "exp(s0)+exp(srel)*x^2",
  par = c(s0 = 1, srel = 0.1),
  plotting = TRUE,
  blather = FALSE,
  ...
)
```

Arguments

data	Reduced replicate data, see reduceReplicates. Need columns "value", "sigma", "n".
factors	'data' is pooled with respect to the columns named here, see Details.
errorModel	Character vector defining the error model in terms of the variance. Use x to reference the independend variable, see Details.
par	Inital values for the parameters of the error model.
plotting	If TRUE, a plot of the pooled variance together with the fit of the error model is shown.
blather	If TRUE, additional information is returned, such as fit parameters and sigmaLS (original sigma given in input data).
...	Parameters handed to the optimizer optim.

Details

The variance estimator using $n-1$ data points is chi^2 distributed with $n-1$ degrees of freedom. Given replicates for consecutive time points, the sample variance can be assumed a function of the sample mean. By defining an error model which must hold for all time points, a maximum likelihood estimator for the parameters of the error model can be derived. The parameter 'errorModel' takes the error model as a character vector, where the mean (independent variable) is refered to as x.

It is desireable to estimate the variance from many replicates. The parameter 'data' must provide one or more columns which define the pooling of data. In case more than one column is announced by 'factors', all combinations are constructed. If, e.g., 'factors = c("condition", "name")' is used, where "condition" is "a", "b", "c" and repeating and "name" is "d", "e" and repeating, the effective conditions used for pooling are "a d", "b e", "c d", "a e", "b d", and "c e".

By default, a plot of the pooled data, sigma and its confidence bound at 68% and 95% is shown.

Value

Returned by default is a data frame with columns as in 'data', but with the sigma values replaced by the derived values, obtained by evaluating the error model with the fit parameters.

If the blather = TRUE option is chosen, fit values of the parameters of the error model are appended, with the column names equal to the parameter names. The error model is appended as the attribute "errorModel". Confidence bounds for sigma at confidence level 68% and 95% are calculated, their values come next in the returned data frame. Finally, the effective conditions are appended to easily check how the pooling was done.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

forcingsSymb *Return some useful forcing functions as strings*

Description

Return some useful forcing functions as strings

Usage

```
forcingsSymb(
  type = c("Gauss", "Fermi", "1-Fermi", "MM", "Signal", "Dose"),
  parameters = NULL
)
```

Arguments

type	Which function to be returned
parameters	Named vector, character or numeric. Replace parameters by the corresponding valus in parameters.

Value

String with the function

format.eqnvec *Encode equation vector in format with sufficient spaces*

Description

Encode equation vector in format with sufficient spaces

Usage

```
## S3 method for class 'eqnvec'
format(x, ...)
```

Arguments

x	object of class eqnvec. Alternatively, a named parsable character vector.
...	additional arguments

Value

named character

funC0 *Evaluation of algebraic expressions defined by characters*

Description

Evaluation of algebraic expressions defined by characters

Usage

```
funC0(
  x,
  variables = getSymbols(x, exclude = parameters),
  parameters = NULL,
  compile = FALSE,
  modelname = NULL,
  verbose = FALSE,
  convenient = TRUE,
  warnings = TRUE
)
```

Arguments

x	Object of class eqnvec or a named character vector with the algebraic expressions
variables	character vector, the symbols that should be treated as variables
parameters	character vector, the symbols that should be treated as parameters
compile	Logical. Directly compile the file. If FALSE and modelname is available, the C file is written but not compiled. In this case, compile has to be called separately to compile one or more .c-files into one .so-file. If modelname is not available, an R function is generated and returned.
modelname	file name of the generated C file. See description of parameter compile.
verbose	Print compiler output to R command line.
convenient	logical, if TRUE return a function with argument . . . to pass all variables/parameters as named arguments
warnings	logical. Suppress warnings about missing variables/parameters that are automatically replaced by zero values.

Value

Either a prediction function f(..., attach.input = FALSE) where the variables/parameters are passed as named arguments or a prediction function f(M, p, attach.input = FALSE) where M is the matrix of variable values (colums with colnames correspond to different variables) and p is the vector of parameter values. The argument attach.input determines whether M is attached to the output. The function f returns a matrix.

Examples

```
library(ggplot2)
myfun <- funC0(c(y = "a*x^4 + b*x^2 + c"))
out <- myfun(a = -1, b = 2, c = 3, x = seq(-2, 2, .1), attach.input = TRUE)
qplot(x = x, y = y, data = as.data.frame(out), geom = "line")
```

---

getCoefficients *Get coefficients from a character*

Description

Get coefficients from a character

Usage

```
getCoefficients(char, symbol)
```

Arguments

char	character, e.g. "2*x + y"
symbol	single character, e.g. "x" or "y"

Value

numeric vector with the coefficients

---

getConditions *Extract the conditions of an object*

Description

Extract the conditions of an object

Usage

```
getConditions(x, ...)

## S3 method for class 'list'
getConditions(x, ...)

## S3 method for class 'fn'
getConditions(x, ...)
```

Arguments

x	object from which the conditions should be extracted
...	additional arguments (not used right now)

Value

The conditions in a format that depends on the class of x.

---

getDerivs *Extract the derivatives of an object*

Description

Extract the derivatives of an object

Usage

```
getDerivs(x, ...)

## S3 method for class 'parvec'
getDerivs(x, ...)

## S3 method for class 'prdframe'
getDerivs(x, ...)

## S3 method for class 'prdlist'
getDerivs(x, ...)

## S3 method for class 'list'
getDerivs(x, ...)

## S3 method for class 'objlist'
getDerivs(x, ...)
```

Arguments

x	object from which the derivatives should be extracted
...	additional arguments (not used right now)

Value

The derivatives in a format that depends on the class of x. This is parvec -> matrix, prdframe -> prdframe, prdlist -> prdlist, objlist -> named numeric.

getEquations *Extract the equations of an object*

Description

Extract the equations of an object

Usage

```
getEquations(x, conditions = NULL)

## S3 method for class 'odemodel'
getEquations(x, conditions = NULL)

## S3 method for class 'prdfn'
getEquations(x, conditions = NULL)

## S3 method for class 'fn'
getEquations(x, conditions = NULL)
```

Arguments

x	object from which the equations should be extracted
conditions	character or numeric vector specifying the conditions to which getEquations is restricted. If conditions has length one, the result is not returned as a list.

Value

The equations as list of eqnvec objects.

getFluxes *Generate list of fluxes from equation list*

Description

Generate list of fluxes from equation list

Usage

```
getFluxes(eqnlist, type = c("conc", "amount"))
```

Arguments

eqnlist	object of class eqnlist.
type	"conc." or "amount" for fluxes in units of concentrations or number of molecules.

Value

list of named characters, the in- and out-fluxes for each state.

Examples

```
# Write your example here. You can also add more Start..End blocks if needed.
# Please mask all output such as print() with the special tag
#
# such that the test is not littered. Statements guarded by  are enabled
# in the example file which is extracted from this test file. To extract the
# example run
#    extractExamples()
# on the R command line.

  ## Generate another equation list
  eq <- eqnlist()
  eq <- addReaction(eq, "A", "pA", "act_A * A * stimulus", "Phosphorylation of A")
  eq <- addReaction(eq, "pA", "A", "deact_A * pA", "Deposphorylation of pA")
 eq <- addReaction(eq, "2*pA", "pA_pA", "form_complex_pA * pA^2", "Complex formation of pA")
  eq <- addReaction(eq, "B", "pB", "act_B * B * pA_pA", "Phosphorylation of B")
  eq <- addReaction(eq, "pB", "B", "deact_B * pB", "Deposphorylation of pB")

  ## Extract data.frame of reactions
  reactions <- getReactions(eq)
   print(reactions)

  ## Get conserved quantities
  cq <- conservedQuantities(eq$smatrix)
   print(cq)

  ## Get fluxes
  fluxes <- getFluxes(eq)
   print(fluxes)

  ## Subsetting of equation list
  subeq1 <- subset(eq, "pB" %in% Product)
   print(subeq1)
  subeq2 <- subset(eq, grepl("not_available", Description))
   print(subeq2)

  ## Time derivatives of observables
  observables <- eqnvec(pA_obs = "s1*pA", tA_obs = "s2*(A + pA)")
  dobs <- dot(observables, eq)

  ## Combined equation vector for ODE and observables
  f <- c(as.eqnvec(eq), dobs)
   print(f)
```

getLocalDLLs *Determine loaded DLLs available in working directory*

Description

Determine loaded DLLs available in working directory

Usage

```
getLocalDLLs()
```

Value

Character vector with the names of the loaded DLLs available in the working directory

getObservables *Extract the observables of an object*

Description

Extract the observables of an object

Usage

```
getObservables(x, ...)
```

Arguments

x	object from which the equations should be extracted
...	not used

Value

The equations as a character.

getParameters *Extract the parameters of an object*

Description

Extract the parameters of an object

Usage

```
getParameters(..., conditions = NULL)

## S3 method for class 'odemodel'
getParameters(x, conditions = NULL)

## S3 method for class 'fn'
getParameters(x, conditions = NULL)

## S3 method for class 'parvec'
getParameters(x, conditions = NULL)

## S3 method for class 'prdframe'
getParameters(x, conditions = NULL)

## S3 method for class 'prdlist'
getParameters(x, conditions = NULL)

## S3 method for class 'eqnlist'
getParameters(x)

## S3 method for class 'eventlist'
getParameters(x)
```

Arguments

...	objects from which the parameters should be extracted
conditions	character vector specifying the conditions to which getParameters is restricted
x	object from which the parameters are extracted

Value

The parameters in a format that depends on the class of x.

getReactions *Generate a table of reactions (data.frame) from an equation list*

Description

Generate a table of reactions (data.frame) from an equation list

Usage

```
getReactions(eqnlist)
```

Arguments

eqnlist	object of class eqnlist

Value

data.frame with educts, products, rate and description. The first column is a check if the reactions comply with reaction kinetics.

Examples

```
# Write your example here. You can also add more Start..End blocks if needed.
# Please mask all output such as print() with the special tag
#
# such that the test is not littered. Statements guarded by  are enabled
# in the example file which is extracted from this test file. To extract the
# example run
#    extractExamples()
# on the R command line.

  ## Generate another equation list
  eq <- eqnlist()
  eq <- addReaction(eq, "A", "pA", "act_A * A * stimulus", "Phosphorylation of A")
  eq <- addReaction(eq, "pA", "A", "deact_A * pA", "Deposphorylation of pA")
 eq <- addReaction(eq, "2*pA", "pA_pA", "form_complex_pA * pA^2", "Complex formation of pA")
  eq <- addReaction(eq, "B", "pB", "act_B * B * pA_pA", "Phosphorylation of B")
  eq <- addReaction(eq, "pB", "B", "deact_B * pB", "Deposphorylation of pB")

  ## Extract data.frame of reactions
  reactions <- getReactions(eq)
   print(reactions)

  ## Get conserved quantities
  cq <- conservedQuantities(eq$smatrix)
   print(cq)

  ## Get fluxes
  fluxes <- getFluxes(eq)
```

```
 print(fluxes)

## Subsetting of equation list
subeq1 <- subset(eq, "pB" %in% Product)
 print(subeq1)
subeq2 <- subset(eq, grepl("not_available", Description))
 print(subeq2)

## Time derivatives of observables
observables <- eqnvec(pA_obs = "s1*pA", tA_obs = "s2*(A + pA)")
dobs <- dot(observables, eq)

## Combined equation vector for ODE and observables
f <- c(as.eqnvec(eq), dobs)
 print(f)
```

---

ggopen *Open last plot in external pdf viewer*

Description

Convenience function to show last plot in an external viewer.

Usage

```
ggopen(plot = last_plot(), command = "xdg-open", ...)
```

Arguments

plot	ggplot2 plot object.
command	character, indicatig which pdf viewer is started.
...	arguments going to ggsave.

Id *An identity function which vanishes upon concatenation of fns*

Description

An identity function which vanishes upon concatenation of fns

Usage

```
Id()
```

Value

fn of class idfn

Examples

```
x <- Xt()
id <- Id()

(id*x)(1:10, pars = c(a = 1))
(x*id)(1:10, pars = c(a = 1))
str(id*x)
str(x*id)
```

---

jakstat *Time-course data for the JAK-STAT cell signaling pathway*

Description

Phosphorylated Epo receptor (pEpoR), phosphorylated STAT in the cytoplasm (tpSTAT) and total STAT (tSTAT) in the cytoplasmhave been measured at times 0, ..., 60.

---

lbind *Bind named list of data.frames into one data.frame*

Description

Bind named list of data.frames into one data.frame

Usage

```
lbind(mylist)
```

Arguments

mylist	A named list of data.frame. The data.frames are expected to have the same structure.

Details

Each data.frame ist augented by a "condition" column containing the name attributed of the list entry. Subsequently, the augmented data.frames are bound together by `rbind`.

Value

data.frame with the originial columns augmented by a "condition" column.

load.parlist *Construct fitlist from temporary files.*

Description

An aborted mstrust leaves behind results of already completed fits. This command loads these fits into a fitlist.

Usage

```
load.parlist(folder)
```

Arguments

folder	Path to the folder where the fit has left its results.

Details

The command mstrust saves each completed fit along the multi-start sequence such that the results can be resurected on abortion. This command loads a fitlist from these intermediate results.

Value

An object of class parlist.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

See Also

mstrust

loadDLL *Load shared object for a dMod object*

Description

Usually when restarting the R session, although all objects are saved in the workspace, the dynamic libraries are not linked any more. loadDLL is a wrapper for dyn.load that uses the "modelname" attribute of dMod objects like prediction functions, observation functions, etc. to load the corresponding shared object.

Usage

```
loadDLL(...)
```

Arguments

...	objects of class prdfn, obsfn, parfn, objfn, ...

---

long2wide *Translate long to wide format (inverse of wide2long.matrix)*

Description

Translate long to wide format (inverse of wide2long.matrix)

Usage

```
long2wide(out)
```

Arguments

out	data.frame in long format

Value

data.frame in wide format

---

lsdMod *Print list of dMod objects in .GlobalEnv*

Description

Lists the objects for a set of classes.

Usage

```
lsdMod(
  classlist = c("odemodel", "parfn", "prdfn", "obsfn", "objfn", "datalist"),
  envir = .GlobalEnv
)
```

Arguments

classlist	List of object classes to print.
envir	Alternative environment to search for objects.

Examples

```
## Not run:
lsdMod()
lsdMod(classlist = "prdfn", envir = environment(obj))

## End(Not run)
```

`match.fnargs` *dMod match function arguments*

Description

The function is exported for dependency reasons

Usage

```
match.fnargs(arglist, choices)
```

Arguments

`arglist`	list
`choices`	character

`mname` *Get modelname from single object (used internally)*

Description

Get modelname from single object (used internally)

Usage

```
mname(x, conditions = NULL)

## S3 method for class '`NULL`'
mname(x, conditions = NULL)

## S3 method for class 'character'
mname(x, conditions = NULL)

## S3 method for class 'objfn'
mname(x, conditions = NULL)

## S3 method for class 'fn'
mname(x, conditions = NULL)
```

Arguments

`x`	dMod object
`conditions`	character vector of conditions

modelname *Get and set modelname*

Description

The modelname attribute refers to the name of a C file associated with a dMod function object like prediction-, parameter transformation- or objective functions.

Usage

```
modelname(..., conditions = NULL)

modelname(x, ...) <- value

## S3 replacement method for class 'fn'
modelname(x, conditions = NULL, ...) <- value

## S3 replacement method for class 'objfn'
modelname(x, conditions = NULL, ...) <- value
```

Arguments

...	objects of type prdfn, parfn, objfn
conditions	character vector of conditions
x	dMod object for which the model name should be set
value	character, the new modelname (does not change the C file)

Value

character vector of model names, corresponding to C files in the local directory.

msParframe *Reproducibly construct "random" parframes*

Description

The output of this function can be used for the center - argument of mstrust

Usage

```
msParframe(pars, n = 20, seed = 12345, samplefun = stats::rnorm, ...)
```

Arguments

pars	Named vector. If samplefun has a "mean"-argument, values of pars will used as mean
n	Integer how many lines should the parframe have
seed	Seed for the random number generator
samplefun	random number generator: rnorm, runif, etc...
...	arguments going to samplefun

Value

parframe (without metanames)

See Also

mstrust and parframe

Examples

```
msParframe(c(a = 0, b = 100000), 5)

# Parameter specific sigma
msParframe(c(a = 0, b = 100000), 5, samplefun = rnorm, sd = c(100, 0.5))
```

---

mstrust *Non-Linear Optimization, multi start*

Description

Wrapper around trust allowing for multiple fits from randomly chosen initial values.

Usage

```
mstrust(
  objfun,
  center,
  studyname,
  rinit = 0.1,
  rmax = 10,
  fits = 20,
  cores = 1,
  samplefun = "rnorm",
  resultPath = ".",
  stats = FALSE,
  output = FALSE,
  ...
)
```

Arguments

objfun	Objective function, see trust.
center	Parameter values around which the initial values for each fit are randomly sampled. The initial values handed to trust are the sum of center and the output of 'samplefun', center + 'samplefun'. See trust, parinit. center Can also be a parframe, then the parameter values are taken from the parframe. In this case, the fits argument is overwritten. To use a reproducible set of initial guesses, generate center with msParframe
studyname	The names of the study or fit. This name is used to determine filenames for interim and final results. See Details.
rinit	Starting trust region radius, see trust.
rmax	Maximum allowed trust region radius, see trust.
fits	Number of fits (jobs).
cores	Number of cores for job parallelization.
samplefun	Function to sample random initial values. It is assumed, that 'samplefun' has a named parameter "n" which defines how many random numbers are to be returned, such as for rnorm or runif. By default rnorm is used. Parameteres for samplefun are simply appended as named parameters to the mstrust call and automatically handed to samplefun by matching parameter names.
resultPath	character indicating the folder where the results should be stored. Defaults to ".".
stats	If true, the same summary statistic as written to the logfile is printed to command line on mstrust completion.
output	logical. If true, writes output to the disc.
...	Additional parameters handed to trust(), samplefun(), or the objective function by matching parameter names. All unmatched parameters are handed to the objective function objfun(). The log file starts with a table telling which parameter was assigend to which function.

Details

By running multiple fits starting at randomly chosen inital parameters, the chisquare landscape can be explored using a deterministic optimizer. Here, trust is used for optimization. The standard procedure to obtain random initial values is to sample random variables from a uniform distribution (rnorm) and adding these to 'center'. It is, however, possible, to employ any other sampling strategy by handing the respective function to mstrust(), 'samplefun'.

In case a special sampling is required, a customized sampling function can be used. If, e.g., inital values leading to a non-physical systems are to be discarded upfront, the objective function can be addapted accordingly.

All started fits either lead to an error or complete converged or unconverged. A statistics about the return status of fits can be shown by setting 'stats' to TRUE.

Fit final and intermediat results are stored under 'studyname'. For each run of mstrust for the same study name, a folder under 'studyname' of the form "trial-x-date" is created. "x" is the number of the trial, date is the current time stamp. In this folder, the intermediate results are stored.

These intermediate results can be loaded by load.parlist. These are removed on successfull completion of mstrust. In this case, the final list of fit parameters (parameterList.Rda) and the fit log (mstrust.log) are found instead.

Value

A parlist holding errored and converged fits.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

See Also

1. trust, for the used optimizer, 2. rnorm, runif for two common sampling functions, 3. msParframe for passing a reproducible set of random initial guesses to mstrust, 4. as.parframe for formatting the output to a handy table

---

nll *Compute the negative log-likelihood*

Description

Compute the negative log-likelihood

Usage

```
nll(nout)
```

Arguments

nout	data.frame (result of res) or object of class objframe.

Value

list with entries value (numeric, the weighted residual sum of squares), gradient (numeric, gradient) and hessian (matrix of type numeric).

normL2 *L2 norm between data and model prediction*

Description

For parameter estimation and optimization, an objective function is needed. normL2 returns an objective function for the L2 norm of data and model prediction. The resulting objective function can be used for optimization with the trust optimizer, see mstrust.

Usage

```
normL2(data, x, errmodel = NULL, times = NULL, attr.name = "data")
```

Arguments

data	object of class datalist
x	object of class prdfn
errmodel	object of class obsfn. errmodel does not need to be defined for all conditions.
times	numeric vector, additional time points where the prediction function is evaluated. If NULL, time points are extacted from the datalist solely. If the prediction function makes use of events, hand over event times here.
attr.name	character. The constraint value is additionally returned in an attributed with this name

Details

Objective functions can be combined by the "+" operator, see sumobjfn.

Value

Object of class obsfn, i.e. a function obj(..., fixed, deriv, conditions, env) that returns an objective list, objlist.

Examples

```
## Generate a prediction function

times <- 0:5
grid <- data.frame(name = "A", time = times, row.names = paste0("p", times))
x <- Xd(grid, condition = "C1")

pars <- structure(rep(0, nrow(grid)), names = row.names(grid))

## Simulate data
data.list <- lapply(1:3, function(i) {
  prediction <- x(times, pars + rnorm(length(pars), 0, 1))
  cbind(wide2long(prediction), sigma = 1)
```

```
})

data <- as.datalist(do.call(rbind, data.list))

## Generate objective function based on data and model
## Then fit the data and plot the result
obj <- normL2(data, x)
myfit <- trust(obj, pars, rinit = 1, rmax = 10)
plot(x(times, myfit$argument), data)
```

`nullZ` *Find integer-null space of matrix A*

Description

Find integer-null space of matrix A

Usage

```
nullZ(A, tol = sqrt(.Machine$double.eps))
```

Arguments

`A`	matrix for which the null space is searched
`tol`	tolerance to find pivots in rref-function below

Value

null space of A with only integers in it

Author(s)

Malenka Mader, <Malenka.Mader@fdm.uni-freiburg.de>

`objframe` *Objective frame*

Description

An objective frame is supposed to store the residuals of a model prediction with respect to a data frame.

Usage

```
objframe(mydata, deriv = NULL, deriv.err = NULL)
```

Arguments

mydata	data.frame as being generated by res.
deriv	matrix of the derivatives of the residuals with respect to parameters.
deriv.err	matrix of the derivatives of the error model.

Value

An object of class objframe, i.e. a data frame with attribute "deriv".

---

objlist *Generate objective list*

Description

An objective list contains an objective value, a gradient, and a Hessian matrix.

Objective lists can contain additional numeric attributes that are preserved or combined with the corresponding attributes of another objective list when both are added by the "+" operator, see sumobjlist.

Objective lists are returned by objective functions as being generated by normL2, constraintL2, priorL2 and datapointL2.

Usage

```
objlist(value, gradient, hessian)
```

Arguments

value	numeric of length 1
gradient	named numeric
hessian	matrix with rownames and colnames according to gradient names

Value

Object of class objlist

obsfn *Observation function*

Description

An observation function is a function is that is concatenated with a prediction function via prodfn to yield a new prediction function, see prdfn. Observation functions are generated by Y. Handling of the conditions is then organized by the obsfn object.

Usage

```
obsfn(X2Y, parameters = NULL, condition = NULL)
```

Arguments

X2Y	the low-level observation function generated e.g. by Y.
parameters	character vector with parameter names
condition	character, the condition name

Details

Observation functions can be "added" by the "+" operator, see sumfn. Thereby, observations for different conditions are merged or, overwritten. Observation functions can also be concatenated with other functions, e.g. observation functions (obsfn) or prediction functions (prdfn) by the "*" operator, see prodfn.

Value

Object of class obsfn, i.e. a function x(..., fixed, deriv, conditions, env) which returns a prdlist. The arguments out (prediction) and pars (parameter values) should be passed via the ... argument.

Examples

```
# Define a time grid on which to make a prediction by peace-wise linear function.
# Then define a (generic) prediction function based on thid grid.
times <- 0:5
grid <- data.frame(name = "A", time = times, row.names = paste0("p", times))
x <- Xd(grid)

# Define an observable and an observation function
observables <- eqnvec(Aobs = "s*A")
g <- Y(g = observables, f = NULL, states = "A", parameters = "s")

# Collect parameters and define an overarching parameter transformation
# for two "experimental condtions".
dynpars <- attr(x, "parameters")
obspars <- attr(g, "parameters")
```

```
innerpars <- c(dynpars, obspars)

trafo <- structure(innerpars, names = innerpars)
trafo_C1 <- replaceSymbols(innerpars, paste(innerpars, "C1", sep = "_"), trafo)
trafo_C2 <- replaceSymbols(innerpars, paste(innerpars, "C2", sep = "_"), trafo)

p <- NULL
p <- p + P(trafo = trafo_C1, condition = "C1")
p <- p + P(trafo = trafo_C2, condition = "C2")

# Collect outer (overarching) parameters and
# initialize with random values
outerpars <- attr(p, "parameters")
pars <- structure(runif(length(outerpars), 0, 1), names = outerpars)

# Predict internal/unobserved states
out1 <- (x*p)(times, pars)
plot(out1)

# Predict observed states in addition to unobserved
out2 <- (g*x*p)(times, pars)
plot(out2)
```

---

odemodel *Generate the model objects for use in Xs (models with sensitivities)*

Description

Generate the model objects for use in Xs (models with sensitivities)

Usage

```
odemodel(
  f,
  deriv = TRUE,
  forcings = NULL,
  events = NULL,
  outputs = NULL,
  fixed = NULL,
  estimate = NULL,
  modelname = "odemodel",
  solver = c("deSolve", "Sundials"),
  gridpoints = NULL,
  verbose = FALSE,
  ...
)
```

Arguments

f	Something that can be converted to eqnvec, e.g. a named character vector with the ODE
deriv	logical, generate sensitivities or not
forcings	Character vector with the names of the forcings
events	data.frame of events with columns "var" (character, the name of the state to be affected), "time" (character or numeric, time point), "value" (character or numeric, value), "method" (character, either "replace" or "add"). See events. Events need to be defined here if they contain parameters, like the event time or value. If both, time and value are purely numeric, they can be specified in Xs(), too.
outputs	Named character vector for additional output variables.
fixed	Character vector with the names of parameters (initial values and dynamic) for which no sensitivities are required (will speed up the integration).
estimate	Character vector specifying parameters (initial values and dynamic) for which sensitivities are returned. If estimate is specified, it overwrites 'fixed'.
modelname	Character, the name of the C file being generated.
solver	Solver for which the equations are prepared.
gridpoints	Integer, the minimum number of time points where the ODE is evaluated internally
verbose	Print compiler output to R command line.
...	Further arguments being passed to funC.

Value

list with func (ODE object) and extended (ODE+Sensitivities object)

Examples

```
## Not run:

## Generate a compiled ODE model from an equation vector
## The model will not return sensitivities for "switch"
## Files will be generated in your working directory!

f <- eqnvec(A = "-k*A + switch*F")
model <- odemodel(f, forcings = "F", fixed = "switch")
print(model)

## Generate the same model from an equation list
f <- addReaction(NULL, from = "", to = "A", rate = "switch*F", description = "production")
f <- addReaction(f   , from = "A", to = "", rate = "k*A", description = "degradation")
print(f)

model <- odemodel(f, forcings = "F", fixed = "switch")
print(model)
```

```
# create forcings
forc1 <- data.frame(name = "F", time = seq(0,5, 0.1), value = sin(seq(0,5,0.1)))
forc2 <- data.frame(name = "F", time = seq(0,5, 0.1), value = exp(-seq(0,5,0.1)))
forc3 <- data.frame(name = "F", time= 0,              value = 0.1)


x <- Xs(model, forc1, condition = "forc1") +
  Xs(model, forc2, condition = "forc2") +
  Xs(model, forc3, condition = "forc3")

g <- Y(c(out1 = "F * A", out2 = "F"), x)

times <-  seq(0,5, 0.001)
pars <- setNames(runif(length(getParameters(x))), getParameters(x))

pred <- (g*x)(times, pars)
plot(pred)



## End(Not run)
```

P *Generate a parameter transformation function*

Description

Generate parameter transformation function from a named character vector or object of class eqnvec. This is a wrapper function for Pexpl and Pimpl. See for more details there.

Usage

```
P(
  trafo = NULL,
  parameters = NULL,
  condition = NULL,
  attach.input = FALSE,
  keep.root = TRUE,
  compile = FALSE,
  modelname = NULL,
  method = c("explicit", "implicit"),
  verbose = FALSE
)
```

Arguments

trafo	object of class eqnvec or named character or list thereof. In case, trafo is a list, P() is called on each element and conditions are assumed to be the list names.
parameters	character vector
condition	character, the condition for which the transformation is generated
attach.input	attach those incoming parameters to output which are not overwritten by the parameter transformation.
keep.root	logical, applies for method = "implicit". The root of the last evaluation of the parameter transformation function is saved as guess for the next evaluation.
compile	logical, compile the function (see funC0)
modelname	character, see funC0
method	character, either "explicit" or "implicit"
verbose	Print out information during compilation

Value

An object of class parfn.

---

parfn *Parameter transformation function*

Description

Generate functions that transform one parameter vector into another by means of a transformation, pushing forward the jacobian matrix of the original parameter. Usually, this function is called internally, e.g. by P. However, you can use it to add your own specialized parameter transformations to the general framework.

Usage

```
parfn(p2p, parameters = NULL, condition = NULL)
```

Arguments

p2p	a transformation function for one condition, i.e. a function p2p(p, fixed, deriv) which translates a parameter vector p and a vector of fixed parameter values fixed into a new parameter vector. If deriv = TRUE, the function should return an attribute deriv with the Jacobian matrix of the parameter transformation.
parameters	character vector, the parameters accepted by the function
condition	character, the condition for which the transformation is defined

Value

object of class parfn, i.e. a function p(..., fixed, deriv, conditions, env). The argument pars should be passed via the ... argument.

Contains attributes "mappings", a list of p2p functions, "parameters", the union of parameters acceted by the mappings and "conditions", the total set of conditions.

See Also

sumfn, P

Examples

```
# Define a time grid on which to make a prediction by peace-wise linear function.
# Then define a (generic) prediction function based on thid grid.
times <- 0:5
grid <- data.frame(name = "A", time = times, row.names = paste0("p", times))
x <- Xd(grid)

# Define an observable and an observation function
observables <- eqnvec(Aobs = "s*A")
g <- Y(g = observables, f = NULL, states = "A", parameters = "s")

# Collect parameters and define an overarching parameter transformation
# for two "experimental condtions".
dynpars <- attr(x, "parameters")
obspars <- attr(g, "parameters")
innerpars <- c(dynpars, obspars)

trafo <- structure(innerpars, names = innerpars)
trafo_C1 <- replaceSymbols(innerpars, paste(innerpars, "C1", sep = "_"), trafo)
trafo_C2 <- replaceSymbols(innerpars, paste(innerpars, "C2", sep = "_"), trafo)

p <- NULL
p <- p + P(trafo = trafo_C1, condition = "C1")
p <- p + P(trafo = trafo_C2, condition = "C2")

# Collect outer (overarching) parameters and
# initialize with random values
outerpars <- attr(p, "parameters")
pars <- structure(runif(length(outerpars), 0, 1), names = outerpars)

# Predict internal/unobserved states
out1 <- (x*p)(times, pars)
plot(out1)

# Predict observed states in addition to unobserved
out2 <- (g*x*p)(times, pars)
plot(out2)
```

parframe *Generate a parameter frame*

Description

A parameter frame is a data.frame where the rows correspond to different parameter specifications. The columns are divided into three parts. (1) the meta-information columns (e.g. index, value, constraint, etc.), (2) the attributes of an objective function (e.g. data contribution and prior contribution) and (3) the parameters.

Usage

```
parframe(
  x = NULL,
  parameters = colnames(x),
  metanames = NULL,
  obj.attributes = NULL
)

is.parframe(x)

## S3 method for class 'parframe'
x[i = NULL, j = NULL, drop = FALSE]

## S3 method for class 'parframe'
subset(x, ...)
```

Arguments

x	data.frame.
parameters	character vector, the names of the parameter columns.
metanames	character vector, the names of the meta-information columns.
obj.attributes	character vector, the names of the objective function attributes.
i	row index in any format
j	column index in any format
drop	logical. If TRUE the result is coerced to the lowest possible dimension
...	additional arguments

Details

Parameter frames can be subsetted either by `[ , ]` or by `subset`. If `[ , index]` is used, the names of the removed columns will also be removed from the corresponding attributes, i.e. metanames, obj.attributes and parameters.

Value

An object of class `parframe`, i.e. a data.frame with attributes for the different names. Inherits from data.frame.

See Also

profile, mstrust

Examples

```
## Generate a prediction function
regfn <- c(y = "sin(a*time)")

g <- Y(regfn, parameters = "a")
x <- Xt(condition = "C1")

## Generate data
data <- datalist(
  C1 = data.frame(
    name = "y",
    time = 1:5,
    value = sin(1:5) + rnorm(5, 0, .1),
    sigma = .1
  )
)

## Initialize parameters and time
pars <- c(a = 1)
times <- seq(0, 5, .1)

plot((g*x)(times, pars), data)

## Do many fits from random positions and store them into parlist
out <- as.parlist(lapply(1:50, function(i) {
  trust(normL2(data, g*x), pars + rnorm(length(pars), 0, 1), rinit = 1, rmax = 10)
}))

summary(out)

## Reduce parlist to parframe
parframe <- as.parframe(out)
plotValues(parframe)

## Reduce parframe to best fit
bestfit <- as.parvec(parframe)
plot((g*x)(times, bestfit), data)
```

parlist *Parameter list*

Description

The special use of a parameter list is to save the outcome of multiple optimization runs provided by mstrust, into one list.

Fitlists carry an fit index which must be held unique on merging multiple fitlists.

Usage

```
parlist(...)

as.parlist(x = NULL)

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

## S3 method for class 'parlist'
c(...)
```

Arguments

...	Objects to be coerced to parameter list.
x	list of lists, as returned by trust
object	a parlist

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

See Also

load.parlist, plot.parlist

Examples

```
## Generate a prediction function
regfn <- c(y = "sin(a*time)")

g <- Y(regfn, parameters = "a")
x <- Xt(condition = "C1")

## Generate data
data <- datalist(
  C1 = data.frame(
    name = "y",
```

```
    time = 1:5,
    value = sin(1:5) + rnorm(5, 0, .1),
    sigma = .1
  )
)

## Initialize parameters and time
pars <- c(a = 1)
times <- seq(0, 5, .1)

plot((g*x)(times, pars), data)

## Do many fits from random positions and store them into parlist
out <- as.parlist(lapply(1:50, function(i) {
  trust(normL2(data, g*x), pars + rnorm(length(pars), 0, 1), rinit = 1, rmax = 10)
}))

summary(out)

## Reduce parlist to parframe
parframe <- as.parframe(out)
plotValues(parframe)

## Reduce parframe to best fit
bestfit <- as.parvec(parframe)
plot((g*x)(times, bestfit), data)
```

---

parvec *Parameter vector*

Description

A parameter vector is a named numeric vector (the parameter values) together with a "deriv" attribute (the Jacobian of a parameter transformation by which the parameter vector was generated).

Usage

```
parvec(..., deriv = NULL)

as.parvec(x, ...)

## S3 method for class 'numeric'
as.parvec(x, names = NULL, deriv = NULL, ...)

## S3 method for class 'parvec'
x[..., drop = FALSE]
```

```
## S3 method for class 'parvec'
c(...)
```

Arguments

`...`	objects to be concatenated
`deriv`	matrix with rownames (according to names of `...`) and colnames according to the names of the parameter by which the parameter vector was generated.
`x`	numeric or named numeric, the parameter values
`names`	optional character vector, the parameter names. Otherwise, names are taken from `x`.
`drop`	logical, drop empty columns in Jacobian after subsetting. ATTENTION: Be careful with this option. The default behavior is to keep the columns in the Jacobian. This can lead to unintended results when subsetting the parvec and using it e.g. in another parameter transformation.

Value

An object of class `parvec`, i.e. a named numeric vector with attribute "deriv".

Examples

```
# Generate a parameter vector
v <- parvec(a = 2, b = 3)
print(v)
print(getDerivs(v))

# Parameter vector from a named numeric
M <- matrix(c(1, 1, 0, 1),
    nrow = 2, ncol = 2,
    dimnames = list(c("a", "b"), c("A", "B"))
    )
v <- as.parvec(x = c(a = 2, b = 3), deriv = M)
print(v)
print(getDerivs(v))

# Subsetting of parameter vectors
# Case 1: Dependencies in the Jacobian are maintained
w <- v[1]
print(w)
print(getDerivs(w))

# Case 2: Dependencies are dropped
w <- v[1, drop = TRUE]
print(w)
print(getDerivs(w))

# Concatenating parameter vectors
w <- parvec(c = 4, d = 5)
print(c(v, w))
print(getDerivs(c(v, w)))
```

Pexpl *Parameter transformation*

Description

Parameter transformation

Usage

```
Pexpl(
  trafo,
  parameters = NULL,
  attach.input = FALSE,
  condition = NULL,
  compile = FALSE,
  modelname = NULL,
  verbose = FALSE
)
```

Arguments

trafo	Named character vector. Names correspond to the parameters being fed into the model (the inner parameters). The elements of tafo are equations that express the inner parameters in terms of other parameters (the outer parameters)
parameters	Character vector. Optional. If given, the generated parameter transformation returns values for each element in parameters. If elements of parameters are not in names(trafo) the identity transformation is assumed.
attach.input	attach those incoming parameters to output which are not overwritten by the parameter transformation.
condition	character, the condition for which the transformation is generated
compile	Logical, compile the function (see funC0)
modelname	Character, used if compile = TRUE, sets a fixed filename for the C file.
verbose	Print compiler output to R command line.

Value

a function p2p(p, fixed = NULL, deriv = TRUE) representing the parameter transformation. Here, p is a named numeric vector with the values of the outer parameters, fixed is a named numeric vector with values of the outer parameters being considered as fixed (no derivatives returned) and deriv is a logical determining whether the Jacobian of the parameter transformation is returned as attribute "deriv".

See Also

Pimpl for implicit parameter transformations

Examples

```
logtrafo <- c(k1 = "exp(logk1)", k2 = "exp(logk2)",
              A = "exp(logA)", B = "exp(logB)")
p_log <- P(logtrafo)

pars <- c(logk1 = 1, logk2 = -1, logA = 0, logB = 0)
out <- p_log(pars)
getDerivs(out)
```

`Pimpl` *Parameter transformation (implicit)*

Description

Parameter transformation (implicit)

Usage

```
Pimpl(
  trafo,
  parameters = NULL,
  condition = NULL,
  keep.root = TRUE,
  positive = TRUE,
  compile = FALSE,
  modelname = NULL,
  verbose = FALSE
)
```

Arguments

`trafo`	Named character vector defining the equations to be set to zero. Names correspond to dependent variables.
`parameters`	Character vector, the independent variables.
`condition`	character, the condition for which the transformation is generated
`keep.root`	logical, applies for `method = "implicit"`. The root of the last evaluation of the parameter transformation function is saved as guess for the next evaluation.
`positive`	logical, returns projection to the (semi)positive range. Comes with a warning if the steady state has been found to be negative.
`compile`	Logical, compile the function (see funC0)
`modelname`	Character, used if `compile = TRUE`, sets a fixed filename for the C file.
`verbose`	Print compiler output to R command line.

Details

Usually, the equations contain the dependent variables, the independent variables and other parameters. The argument p of p2p must provide values for the independent variables and the parameters but ALSO FOR THE DEPENDENT VARIABLES. Those serve as initial guess for the dependent variables. The dependent variables are then numerically computed by multiroot. The Jacobian of the solution with respect to dependent variables and parameters is computed by the implicit function theorem. The function p2p returns all parameters as they are with corresponding 1-entries in the Jacobian.

Value

a function `p2p(p, fixed = NULL, deriv = TRUE)` representing the parameter transformation. Here, `p` is a named numeric vector with the values of the outer parameters, `fixed` is a named numeric vector with values of the outer parameters being considered as fixed (no derivatives returned) and `deriv` is a logical determining whether the Jacobian of the parameter transformation is returned as attribute "deriv".

See Also

Pexpl for explicit parameter transformations

Examples

```
##############################################################################
## Example 1: Steady-state trafo
##############################################################################
f <- c(A = "-k1*A + k2*B",
       B = "k1*A - k2*B")
P.steadyState <- Pimpl(f, "A")

p.outerValues <- c(k1 = 1, k2 = 0.1, A = 10, B = 1)
P.steadyState(p.outerValues)

##############################################################################
## Example 2: Steady-state trafo combined with log-transform
##############################################################################
f <- c(A = "-k1*A + k2*B",
       B = "k1*A - k2*B")
P.steadyState <- Pimpl(f, "A")

logtrafo <- c(k1 = "exp(logk1)", k2 = "exp(logk2)", A = "exp(logA)", B = "exp(logB)")
P.log <- P(logtrafo)

p.outerValue <- c(logk1 = 1, logk2 = -1, logA = 0, logB = 0)
(P.log)(p.outerValue)
(P.steadyState * P.log)(p.outerValue)

##############################################################################
## Example 3: Steady-states with conserved quantitites
##############################################################################
f <- c(A = "-k1*A + k2*B", B = "k1*A - k2*B")
```

```
replacement <- c(B = "A + B - total")
f[names(replacement)] <- replacement

pSS <- Pimpl(f, "total")
pSS(c(k1 = 1, k2 = 2, A = 5, B = 5, total = 3))
```

`plot.datalist` *Plot a list data points*

Description

Plot a list data points

Usage

```
## S3 method for class 'datalist'
plot(x, ..., scales = "free", facet = "wrap")
```

Arguments

`x`	Named list of data.frames as being used in res, i.e. with columns `name`, `time`, `value` and `sigma`.
`...`	Further arguments going to `dplyr::filter`.
`scales`	The scales argument of `facet_wrap` or `facet_grid`, i.e. `"free"`, `"fixed"`, `"free_x"` or `"free_y"`
`facet`	Either `"wrap"` or `"grid"`

Details

The data.frame being plotted has columns `time`, `value`, `sigma`, `name` and `condition`.

Value

A plot object of class `ggplot`.

plot.parlist *Plot a parameter list.*

Description

Plot a parameter list.

Usage

```
## S3 method for class 'parlist'
plot(x, path = FALSE, ...)
```

Arguments

x	fitlist obtained from mstrust
path	print path of parameters from initials to convergence. For this option to be TRUE mstrust must have had the option 'blather'.
...	additional arguments

Details

If path=TRUE:

Author(s)

Malenka Mader, <Malenka.Mader@fdm.uni-freiburg.de>

plotCombined *Plot a list of model predictions and a list of data points in a combined plot*

Description

Plot a list of model predictions and a list of data points in a combined plot

Usage

```
plotCombined(prediction, ...)

## S3 method for class 'prdlist'
plot(x, data = NULL, ..., scales = "free", facet = "wrap", transform = NULL)

## S3 method for class 'prdlist'
plotCombined(
  prediction,
```

```
  data = NULL,
  ...,
  scales = "free",
  facet = "wrap",
  transform = NULL,
  aesthetics = NULL
)

## S3 method for class 'prdframe'
plot(x, data = NULL, ..., scales = "free", facet = "wrap", transform = NULL)
```

Arguments

prediction	Named list of matrices or data.frames, usually the output of a prediction function as generated by Xs.
...	Further arguments going to dplyr::filter.
x	prediction
data	Named list of data.frames as being used in res, i.e. with columns name, time, value and sigma.
scales	The scales argument of facet_wrap or facet_grid, i.e. "free", "fixed", "free_x" or "free_y"
facet	"wrap" or "grid". Try "wrap_plain" for high amounts of conditions and low amounts of observables.
transform	list of transformation for the states, see coordTransform.
aesthetics	Named list of aesthetic mappings, specified as character, e.g. list(linetype = "name"). Can refer to variables in the condition.grid

Details

The data.frame being plotted has columns time, value, sigma, name and condition.

Value

A plot object of class ggplot.

Examples

```
## Observation function
fn <- eqnvec(
  sine = "1 + sin(6.28*omega*time)",
  cosine = "cos(6.28*omega*time)"
)
g <- Y(fn, parameters = "omega")

## Prediction function for time
x <- Xt()
```

```
## Parameter transformations to split conditions
p <- NULL
for (i in 1:3) {
 p <- p + P(trafo = c(omega = paste0("omega_", i)), condition = paste0("frequency_", i))
}

## Evaluate prediction
times <- seq(0, 1, .01)
pars <- structure(seq(1, 2, length.out = 3), names = attr(p, "parameters"))

prediction <- (g*x*p)(times, pars)

## Plotting prediction
# plot(prediction)
plotPrediction(prediction)
plotPrediction(prediction, scales = "fixed")
plotPrediction(prediction, facet = "grid")
plotPrediction(prediction,
               scales = "fixed",
               transform = list(sine = "x^2", cosine = "x - 1"))

## Simulate data
dataset <- wide2long(prediction)
dataset <- dataset[seq(1, nrow(dataset), 5),]
set.seed(1)
dataset$value <- dataset$value + rnorm(nrow(dataset), 0, .1)
dataset$sigma <- 0.1
data <- as.datalist(dataset, split.by = "condition")

## Plotting data
# plot(data)
plot1 <- plotData(data)
 plot1
## Plotting data and prediction with subsetting
# plot(prediction, data)
plot2 <- plotCombined(prediction, data)
 plot2
plot3 <- plotCombined(prediction, data,
             time <= 0.5 & condition == "frequency_1")
 plot3
plot4 <- plotCombined(prediction, data,
             time <= 0.5 & condition != "frequency_1",
             facet = "grid")
 plot4
plot5 <- plotCombined(prediction, data, aesthetics = list(linetype = "condition"))
 plot5
```

`plotData.datalist` *Plot a list data points*

Description

Plot a list data points

Usage

```
## S3 method for class 'datalist'
plotData(data, ..., scales = "free", facet = "wrap", transform = NULL)

plotData(data, ...)

## S3 method for class 'data.frame'
plotData(data, ...)
```

Arguments

data	Named list of data.frames as being used in res, i.e. with columns name, time, value and sigma.
...	Further arguments going to subset.
scales	The scales argument of facet_wrap or facet_grid, i.e. "free", "fixed", "free_x" or "free_y"
facet	Either "wrap" or "grid"
transform	list of transformation for the states, see coordTransform.

Details

The data.frame being plotted has columns time, value, sigma, name and condition.

Value

A plot object of class ggplot.

Examples

```
## Observation function
fn <- eqnvec(
  sine = "1 + sin(6.28*omega*time)",
  cosine = "cos(6.28*omega*time)"
)
g <- Y(fn, parameters = "omega")

## Prediction function for time
x <- Xt()

## Parameter transformations to split conditions
p <- NULL
for (i in 1:3) {
 p <- p + P(trafo = c(omega = paste0("omega_", i)), condition = paste0("frequency_", i))
}
```

```
## Evaluate prediction
times <- seq(0, 1, .01)
pars <- structure(seq(1, 2, length.out = 3), names = attr(p, "parameters"))

prediction <- (g*x*p)(times, pars)

## Plotting prediction
# plot(prediction)
plotPrediction(prediction)
plotPrediction(prediction, scales = "fixed")
plotPrediction(prediction, facet = "grid")
plotPrediction(prediction,
               scales = "fixed",
               transform = list(sine = "x^2", cosine = "x - 1"))

## Simulate data
dataset <- wide2long(prediction)
dataset <- dataset[seq(1, nrow(dataset), 5),]
set.seed(1)
dataset$value <- dataset$value + rnorm(nrow(dataset), 0, .1)
dataset$sigma <- 0.1
data <- as.datalist(dataset, split.by = "condition")

## Plotting data
# plot(data)
plot1 <- plotData(data)
 plot1
## Plotting data and prediction with subsetting
# plot(prediction, data)
plot2 <- plotCombined(prediction, data)
 plot2
plot3 <- plotCombined(prediction, data,
             time <= 0.5 & condition == "frequency_1")
 plot3
plot4 <- plotCombined(prediction, data,
             time <= 0.5 & condition != "frequency_1",
             facet = "grid")
 plot4
plot5 <- plotCombined(prediction, data, aesthetics = list(linetype = "condition"))
 plot5
```

`plotFluxes` *Plot Fluxes given a list of flux Equations*

Description

Plot Fluxes given a list of flux Equations

Usage

```
plotFluxes(pouter, x, times, fluxEquations, nameFlux = "Fluxes:", ...)
```

Arguments

pouter	parameters
x	The model prediction function x(times, pouter, fixed, ...)
times	Numeric vector of time points for the model prediction
fluxEquations	list of chars containing expressions for the fluxes, if names are given, they are shown in the legend. Easy to obtain via subset.eqnlist, see Examples.
nameFlux	character, name of the legend.
...	Further arguments going to x, such as fixed or conditions

Value

A plot object of class ggplot.

Examples

```
## Not run:

plotFluxes(bestfit, x, times, subset(f, "B"%in%Product)$rates, nameFlux = "B production")

## End(Not run)
```

---

plotPars.parframe *Plot parameter values for a fitlist*

Description

Plot parameter values for a fitlist

Usage

```
## S3 method for class 'parframe'
plotPars(x, tol = 1, ...)

plotPars(x, ...)
```

Arguments

x	parameter frame as obtained by as.parframe(mstrust)
tol	maximal allowed difference between neighboring objective values to be recognized as one.
...	arguments for subsetting of x

plotPaths *Profile likelihood: plot of the parameter paths.*

Description

Profile likelihood: plot of the parameter paths.

Usage

```
plotPaths(
  profs,
  ...,
  whichPar = NULL,
  sort = FALSE,
  relative = TRUE,
  scales = "fixed"
)
```

Arguments

profs	profile or list of profiles as being returned by profile
...	arguments going to subset
whichPar	Character or index vector, indicating the parameters that are taken as possible reference (x-axis)
sort	Logical. If paths from different parameter profiles are plotted together, possible combinations are either sorted or all combinations are taken as they are.
relative	logical indicating whether the origin should be shifted.
scales	character, either "free" or "fixed".

Details

See profile for examples.

Value

A plot object of class ggplot.

plotPrediction *Plot a list of model predictions*

Description

Plot a list of model predictions

Usage

```
plotPrediction(prediction, ...)

## S3 method for class 'prdlist'
plotPrediction(
  prediction,
  ...,
  errfn = NULL,
  scales = "free",
  facet = "wrap",
  transform = NULL
)
```

Arguments

prediction	Named list of matrices or data.frames, usually the output of a prediction function as generated by Xs.
...	Further arguments going to dplyr::filter.
errfn	error model function
scales	The scales argument of facet_wrap or facet_grid, i.e. "free", "fixed", "free_x" or "free_y"
facet	Either "wrap" or "grid"
transform	list of transformation for the states, see coordTransform.

Details

The data.frame being plotted has columns time, value, name and condition.

Value

A plot object of class ggplot.

Examples

```
## Observation function
fn <- eqnvec(
  sine = "1 + sin(6.28*omega*time)",
```

```
  cosine = "cos(6.28*omega*time)"
)
g <- Y(fn, parameters = "omega")

## Prediction function for time
x <- Xt()

## Parameter transformations to split conditions
p <- NULL
for (i in 1:3) {
p <- p + P(trafo = c(omega = paste0("omega_", i)), condition = paste0("frequency_", i))
}

## Evaluate prediction
times <- seq(0, 1, .01)
pars <- structure(seq(1, 2, length.out = 3), names = attr(p, "parameters"))

prediction <- (g*x*p)(times, pars)

## Plotting prediction
# plot(prediction)
plotPrediction(prediction)
plotPrediction(prediction, scales = "fixed")
plotPrediction(prediction, facet = "grid")
plotPrediction(prediction,
               scales = "fixed",
               transform = list(sine = "x^2", cosine = "x - 1"))

## Simulate data
dataset <- wide2long(prediction)
dataset <- dataset[seq(1, nrow(dataset), 5),]
set.seed(1)
dataset$value <- dataset$value + rnorm(nrow(dataset), 0, .1)
dataset$sigma <- 0.1
data <- as.datalist(dataset, split.by = "condition")

## Plotting data
# plot(data)
plot1 <- plotData(data)
 plot1
## Plotting data and prediction with subsetting
# plot(prediction, data)
plot2 <- plotCombined(prediction, data)
 plot2
plot3 <- plotCombined(prediction, data,
             time <= 0.5 & condition == "frequency_1")
 plot3
plot4 <- plotCombined(prediction, data,
             time <= 0.5 & condition != "frequency_1",
             facet = "grid")
 plot4
plot5 <- plotCombined(prediction, data, aesthetics = list(linetype = "condition"))
 plot5
```

`plotProfile.parframe` *Profile likelihood plot*

Description

Profile likelihood plot

Usage

```
## S3 method for class 'parframe'
plotProfile(profs, ..., maxvalue = 5, parlist = NULL)

## S3 method for class 'list'
plotProfile(profs, ..., maxvalue = 5, parlist = NULL)

plotProfile(profs, ...)
```

Arguments

`profs`	Lists of profiles as being returned by profile.
`...`	logical going to subset before plotting.
`maxvalue`	Numeric, the value where profiles are cut off.
`parlist`	Matrix or data.frame with columns for the parameters to be added to the plot as points. If a "value" column is contained, deltas are calculated with respect to lowest chisquare of profiles.

Details

See profile for examples.

Value

A plot object of class `ggplot`.

plotResiduals *Plot residuals for a fitlist*

Description

Plot residuals for a fitlist

Usage

```
plotResiduals(parframe, x, data, split = "condition", errmodel = NULL, ...)
```

Arguments

parframe	Object of class parframe, e.g. returned by mstrust
x	Prediction function returning named list of data.frames with names as data.
data	Named list of data.frames, i.e. with columns name, time, value and sigma.
split	List of characters specifying how to summarise the residuals by sqrt(res_i^2), split[1] used for x-axis, split[2] for grouping (color), and any additional for facet_wrap()
errmodel	object of type prdfn, the error model function.
...	Additional arguments for x

Value

A plot object of class ggplot with data.frame as attribute attr(P,"out").

Examples

```
## Not run:
 # time axis:
 plotResiduals(myfitlist, g*x*p, data,
    c("time","index","condition","name"),
    conditions = myconditions[1:4])
 # condition axis (residuals summed over time for each observable and condition):
 plotResiduals(myfitlist, g*x*p, data,  c("condition","name","index"))

## End(Not run)
```

plotValues.parframe *Plotting objective values of a collection of fits*

Description

Plotting objective values of a collection of fits

Usage

```
## S3 method for class 'parframe'
plotValues(x, tol = 1, ...)

plotValues(x, ...)
```

Arguments

x	data.frame with columns "value", "converged" and "iterations", e.g. a parframe.
tol	maximal allowed difference between neighboring objective values to be recognized as one.
...	arguments for subsetting of x

prdfn *Prediction function*

Description

A prediction function is a function `x(..., fixed, deriv, conditions)`. Prediction functions are generated by Xs, Xf or Xd. For an example see the last one.

Usage

```
prdfn(P2X, parameters = NULL, condition = NULL)
```

Arguments

P2X	transformation function as being produced by Xs.
parameters	character vector with parameter names
condition	character, the condition name

Details

Prediction functions can be "added" by the "+" operator, see sumfn. Thereby, predictions for different conditions are merged or overwritten. Prediction functions can also be concatenated with other functions, e.g. observation functions (obsfn) or parameter transformation functions (parfn) by the "*" operator, see prodfn.

Value

Object of class prdfn, i.e. a function x(..., fixed, deriv, conditions, env) which returns a prdlist. The arguments times and pars (parameter values) should be passed via the ... argument, in this order.

Examples

```
# Define a time grid on which to make a prediction by peace-wise linear function.
# Then define a (generic) prediction function based on thid grid.
times <- 0:5
grid <- data.frame(name = "A", time = times, row.names = paste0("p", times))
x <- Xd(grid)

# Define an observable and an observation function
observables <- eqnvec(Aobs = "s*A")
g <- Y(g = observables, f = NULL, states = "A", parameters = "s")

# Collect parameters and define an overarching parameter transformation
# for two "experimental condtions".
dynpars <- attr(x, "parameters")
obspars <- attr(g, "parameters")
innerpars <- c(dynpars, obspars)

trafo <- structure(innerpars, names = innerpars)
trafo_C1 <- replaceSymbols(innerpars, paste(innerpars, "C1", sep = "_"), trafo)
trafo_C2 <- replaceSymbols(innerpars, paste(innerpars, "C2", sep = "_"), trafo)

p <- NULL
p <- p + P(trafo = trafo_C1, condition = "C1")
p <- p + P(trafo = trafo_C2, condition = "C2")

# Collect outer (overarching) parameters and
# initialize with random values
outerpars <- attr(p, "parameters")
pars <- structure(runif(length(outerpars), 0, 1), names = outerpars)

# Predict internal/unobserved states
out1 <- (x*p)(times, pars)
plot(out1)

# Predict observed states in addition to unobserved
out2 <- (g*x*p)(times, pars)
plot(out2)
```

---

prdframe *Prediction frame*

Description

A prediction frame is used to store a model prediction in a matrix. The columns of the matrix are "time" and one column per state. The prediction frame has attributes "deriv", the matrix of sensitivities with respect to "outer parameters" (see P), an attribute "sensitivities", the matrix of sensitivities with respect to the "inner parameters" (the model parameters, left-hand-side of the parameter transformation) and an attributes "parameters", the parameter vector of inner parameters to produce the prediction frame.

Prediction frames are usually the constituents of prediction lists (prdlist). They are produced by Xs, Xd or Xf. When you define your own prediction functions, see `P2X` in prdfn, the result should be returned as a prediction frame.

Usage

```
prdframe(
  prediction = NULL,
  deriv = NULL,
  sensitivities = NULL,
  parameters = NULL
)
```

Arguments

`prediction`	matrix of model prediction
`deriv`	matrix of sensitivities wrt outer parameters
`sensitivities`	matrix of sensitivitie wrt inner parameters
`parameters`	names of the outer paramters

Value

Object of class `prdframe`, i.e. a matrix with other matrices and vectors as attributes.

`prdlist` *Prediction list*

Description

A prediction list is used to store a list of model predictions from different prediction functions or the same prediction function with different parameter specifications. Each entry of the list is a prdframe.

Usage

```
prdlist(...)

as.prdlist(x, ...)

## S3 method for class 'list'
as.prdlist(x = NULL, names = NULL, ...)
```

Arguments

...	objects of class prdframe conditions.
x	list of prediction frames
names	character vector, the list names, e.g. the names of the experimental

---

`predict.prdfn` *Model Predictions*

Description

Make a model prediction for times and a parameter frame. The function is a generalization of the standard prediction by a prediction function object in that it allows to pass a parameter frame instead of a single parameter vector.

Usage

```
## S3 method for class 'prdfn'
predict(object, ..., times, pars, data = NULL)
```

Arguments

object	prediction function
...	Further arguments goint to the prediction function
times	numeric vector of time points
pars	parameter frame, e.g. output from mstrust or profile
data	data list object. If data is passed, its condition.grid attribute is used to augment the output dataframe by additional columns. "data" itself is returned as an attribute.

Value

A data frame

print.eqnlist *Print or pander equation list*

Description

Print or pander equation list

Usage

```
## S3 method for class 'eqnlist'
print(x, pander = FALSE, ...)
```

Arguments

x	object of class eqnlist
pander	logical, use pander for output (used with R markdown)
...	additional arguments

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

Daniel Kaschek, <daniel.kaschek@physik.uni-freiburg.de>

print.eqnvec *Print equation vector*

Description

Print equation vector

Usage

```
## S3 method for class 'eqnvec'
print(x, width = 140, pander = FALSE, ...)
```

Arguments

x	object of class eqnvec.
width	numeric, width of the print-out
pander	logical, use pander for output (used with R markdown)
...	not used right now

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

print.parfn *Pretty printing parameter transformations*

Description

Pretty printing parameter transformations

Usage

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

Arguments

x	prediction function
...	additional arguments

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

print.parvec *Pretty printing for a parameter vector*

Description

Pretty printing for a parameter vector

Usage

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

Arguments

x	object of class parvec
...	not used yet.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

print0 *Print object and its "default" attributes only.*

Description

Print object and its "default" attributes only.

Usage

```
print0(x, list_attributes = TRUE)
```

Arguments

x	Object to be printed
list_attributes	Prints the names of all attribute of x, defaults to TRUE

Details

Before the 'x' is printed by print.default, all its arguments not in the default list of attrs are removed.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

Mirjam Fehling-Kaschek, <mirjam.fehling@physik.uni-freiburg.de>

priorL2 *L2 objective function for prior value*

Description

As a prior function, it returns derivatives with respect to the penalty parameter in addition to parameter derivatives.

Usage

```
priorL2(mu, lambda = "lambda", attr.name = "prior", condition = NULL)
```

Arguments

mu	Named numeric, the prior values
lambda	Character of length one. The name of the penalty paramter in p.
attr.name	character. The constraint value is additionally returned in an attributed with this name
condition	character, the condition for which the constraint should apply. If NULL, applies to any condition.

Details

Computes the constraint value

$$e^{\lambda}\|p-\mu\|^2$$

and its derivatives with respect to p and lambda.

Value

List of class `objlist`, i.e. objective value, gradient and Hessian as list.

See Also

wrss

Examples

```
p <- c(A = 1, B = 2, C = 3, lambda = 0)
mu <- c(A = 0, B = 0)
obj <- priorL2(mu = mu, lambda = "lambda")
obj(pars = p + rnorm(length(p), 0, .1))
```

---

profile *Profile-likelihood (PL) computation*

Description

Profile-likelihood (PL) computation

Usage

```
profile(
  obj,
  pars,
  whichPar,
  alpha = 0.05,
  limits = c(lower = -Inf, upper = Inf),
  method = c("integrate", "optimize"),
  stepControl = NULL,
  algoControl = NULL,
  optControl = NULL,
  verbose = FALSE,
  cores = 1,
  ...
)
```

Arguments

obj	Objective function obj(pars, fixed, ...) returning a list with "value", "gradient" and "hessian". If attribute "valueData" and/or "valuePrior are returned they are attached to the return value.
pars	Parameter vector corresponding to the log-liklihood optimum.
whichPar	Numeric or character vector. The parameters for which the profile is computed.
alpha	Numeric, the significance level based on the chisquare distribution with df=1
limits	Numeric vector of length 2, the lower and upper deviance from the original value of pars[whichPar]
method	Character, either "integrate" or "optimize". This is a short-cut for setting stepControl, algoControl and optControl by hand.
stepControl	List of arguments controlling the step adaption. Defaults to integration set-up, i.e. list(stepsize = 1e-4, min = 1e-4, max = Inf, atol = 1e-2, rtol = 1e-2, limit = 100)
algoControl	List of arguments controlling the fast PL algorithm. defaults to list(gamma = 1, W = "hessian", reoptimize = FALSE, correction = 1, reg = .Machine$double.eps)
optControl	List of arguments controlling the trust() optimizer. Defaults to list(rinit = .1, rmax = 10, iterlim = 10, fterm = sqrt(.Machine$double.eps), mterm = sqrt(.Machine$double.eps)). See trust for more details.
verbose	Logical, print verbose messages.
cores	number of cores used when computing profiles for several parameters.
...	Arguments going to obj()

Details

Computation of the profile likelihood is based on the method of Lagrangian multipliers and Euler integration of the corresponding differential equation of the profile likelihood paths.

algoControl: Since the Hessian which is needed for the differential equation is frequently misspecified, the error in integration needs to be compensated by a correction factor gamma. Instead of the Hessian, an identity matrix can be used. To guarantee that the profile likelihood path stays on the true path, each point proposed by the differential equation can be used as starting point for an optimization run when reoptimize = TRUE. The correction factor gamma is adapted based on the amount of actual correction. If this exceeds the value correction, gamma is reduced. In some cases, the Hessian becomes singular. This leads to problems when inverting the Hessian. To avoid this problem, the pseudoinverse is computed by removing all singular values lower than reg.

stepControl: The Euler integration starts with stepsize. In each step the predicted change of the objective function is compared with the actual change. If this is larger than atol, the stepsize is reduced. For small deviations, either compared the abolute tolerance atol or the relative tolerance rtol, the stepsize may be increased. max and min are upper and lower bounds for stepsize. limit is the maximum number of steps that are take for the profile computation. stop is a character, usually "value" or "data", for which the significance level alpha is evaluated.

Value

Named list of length one. The name is the parameter name. The list enty is a matrix with columns "value" (the objective value), "constraint" (deviation of the profiled paramter from the original value), "stepsize" (the stepsize take for the iteration), "gamma" (the gamma value employed for the iteration), "valueData" and "valuePrior" (if specified in obj), one column per parameter (the profile paths).

Examples

```
## Not run:

## Parameter transformation
trafo <- eqnvec(a = "exp(loga)",
                b = "exp(logb)",
                c = "exp(loga)*exp(logb)*exp(logc)")
p <- P(trafo)

## Objective function
obj1 <- constraintL2(mu = c(a = .1, b = 1, c = 10), sigma = .6)
obj2 <- constraintL2(mu = c(loga = 0, logb = 0), sigma = 10)
obj <- obj1*p + obj2

## Initialize parameters and obtain fit
pars <- c(loga = 1, logb = 1, logc = 1)
myfit <- trust(obj, pars, rinit = 1, rmax = 10)
myfit.fixed <- trust(obj, pars[-1], rinit = 1, rmax = 10, fixed = pars[1])

## Compute profiles by integration method
profiles.approx <- do.call(
  rbind,
  lapply(1:3, function(i) {
    profile(obj, myfit$argument, whichPar = i, limits = c(-3, 3),
            method = "integrate")
  })
)

## Compute profiles by repeated optimization
profiles.exact <- do.call(
  rbind,
  lapply(1:3, function(i) {
    profile(obj, myfit$argument, whichPar = i, limits = c(-3, 3),
            method = "optimize")
  })
)

## Compute profiles for fit with fixed element by integration method
profiles.approx.fixed <- do.call(
  rbind,
  lapply(1:2, function(i) {
    profile(obj, myfit.fixed$argument, whichPar = i, limits = c(-3, 3),
            method = "integrate",
            fixed = pars[1])
```

```
  })
)

## Plotting
plotProfile(profiles.approx)
plotProfile(list(profiles.approx, profiles.exact))
plotProfile(list(profiles.approx, profiles.approx.fixed))

plotPaths(profiles.approx, sort = TRUE)
plotPaths(profiles.approx, whichPar = "logc")
plotPaths(list(profiles.approx, profiles.approx.fixed), whichPar = "logc")

## Confidence Intervals
confint(profiles.approx, val.column = "value")


## End(Not run)
```

`progressBar` *Progress bar*

Description

Progress bar

Usage

```
progressBar(percentage, size = 50, number = TRUE)
```

Arguments

`percentage`	Numeric between 0 and 100
`size`	Integer, the size of the bar print-out
`number`	Logical, Indicates whether the percentage should be printed out.

`reduceReplicates` *Reduce replicated measurements to mean and standard deviation*

Description

Obtain the mean and standard deviation from replicates per condition.

Usage

```
reduceReplicates(file, select = "condition", datatrans = NULL)
```

Arguments

`file`	Data file of csv. See Format for details.
`select`	Names of the columns in the data file used to define conditions, see Details.
`datatrans`	Character vector describing a function to transform data. Use `x` to refere to data.

Format

The following columns are mandatory for the data file.

name Name of the observed species.

time Measurement time point.

value Measurement value.

condition The condition under which the observation was made.

In addition to these columns, any number of columns can follow to allow a fine grained definition of conditions. The values of all columns named in '`select`' are then merged to get the set of conditions.

Details

Experiments are usually repeated multiple times possibly under different conditions leading to replicted measurements. The column "Condition" in the data allows to group the data by their condition. However, sometimes, a more fine grained grouping is desirable. In this case, any number of additional columns can be append to the data. These columns are referred to as "condition identifier". Which of the condition identifiers are used to do the grouping is user defined by anouncing the to '`select`'. The mandatory column "Condition" is always used. The total set of different conditions is thus defined by all combinations of values occuring in the selected condition identifiers. The replicates of each condition are then reduced to mean and variance.New conditions names are derived by merging all conditions which were used in mean and std.

Value

A data frame of the following variables

time Measurement time point.

name Name of the observed species.

value Mean of replicates.

sigma Standard error of the mean, NA for single measurements.

n The number of replicates reduced.

condition The condition for which the value and sigma were calculated. If more than one column were used to define the condition, this variable holds the effecive condition which is the combination of all applied single conditions.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

repar *Reparameterization*

Description

Reparameterization

Usage

```
repar(expr, trafo = NULL, ..., reset = FALSE)
```

Arguments

expr	character of the form "lhs ~ rhs" where rhs reparameterizes lhs. Both lhs and rhs can contain a number of symbols whose values need to be passed by the ... argument.
trafo	character or equation vector or list thereof. The object where the replacement takes place in
...	pass symbols as named arguments
reset	logical. If true, the trafo element corresponding to lhs is reset according to rhs. If false, lhs wherever it occurs in the rhs of trafo is replaced by rhs of the formula.

Details

Left and right-hand side of expr are searched for symbols. If separated by "_", symbols are recognized as such, e.g. in Delta_x where the symbols are "Delta" and "x". Each symbol for which values (character or numbers) are passed by the ... argument is replaced.

Value

an equation vector with the reparameterization.

Examples

```
innerpars <- letters[1:3]
constraints <- c(a = "b + c")
mycondition <- "cond1"

trafo <- repar("x ~ x", x = innerpars)
trafo <- repar("x ~ y", trafo, x = names(constraints), y = constraints)
trafo <- repar("x ~ exp(x)", trafo, x = innerpars)
trafo <- repar("x ~ x + Delta_x_condition", trafo, x = innerpars, condition = mycondition)
```

res *Compare data and model prediction by computing residuals*

Description

Compare data and model prediction by computing residuals

Usage

```
res(data, out, err = NULL)
```

Arguments

data	data.frame with name (factor), time (numeric), value (numeric) and sigma (numeric)
out	output of ode(), optionally augmented with attributes "deriv" (output of ode() for the sensitivity equations) and "parameters" (character vector of parameter names, a subsest of those contained in the sensitivity equations). If "deriv" is given, also "parameters" needs to be given.
err	output of the error model function

Value

data.frame with the original data augmented by columns "prediction" (numeric, the model prediction), "residual" (numeric, difference between prediction and data value), "weighted.residual" (numeric, residual devided by sigma). If "deriv" was given, the returned data.frame has an attribute "deriv" (data.frame with the derivatives of the residuals with respect to the parameters).

resolveRecurrence *Place top elements into bottom elemens*

Description

Place top elements into bottom elemens

Usage

```
resolveRecurrence(variables)
```

Arguments

variables	named character vector

Details

If the names of top vector elements occur in the bottom of the vector, they are replaced by the character of the top entry. Useful for steady state conditions.

Value

named character vector of the same length as `variables`

Examples

```
resolveRecurrence(c(A = "k1*B/k2", C = "A*k3+k4", D="A*C*k5"))
```

---

rref *Transform matrix A into reduced row echelon form this function is written along the lines of the rref-matlab function.*

Description

Transform matrix A into reduced row echelon form this function is written along the lines of the rref-matlab function.

Usage

```
rref(A, tol = sqrt(.Machine$double.eps), verbose = FALSE, fractions = FALSE)
```

Arguments

`A`	matrix for which the reduced row echelon form is searched
`tol`	tolerance to find pivots
`verbose`	logical, print verbose information
`fractions`	logical, not used right now.

Value

a list of two entries is returned; ret[[1]] is the reduced row echelon form of A, ret[[2]] is the index of columns in which a pivot was found

Author(s)

Malenka Mader, <Malenka.Mader@fdm.uni-freiburg.de>

scale_color_dMod *Standard dMod color palette*

Description

Standard dMod color palette

Usage

```
scale_color_dMod(...)
```

Arguments

...	arguments goint to codescale_color_manual()

Examples

```
library(ggplot2)
times <- seq(0, 2*pi, 0.1)
values <- sin(times)
data <- data.frame(
   time = times,
   value = c(values, 1.2*values, 1.4*values, 1.6*values),
   group = rep(c("C1", "C2", "C3", "C4"), each = length(times))
)
qplot(time, value, data = data, color = group, geom = "line") +
   theme_dMod() + scale_color_dMod()
```

scale_fill_dMod *Standard dMod color scheme*

Description

Standard dMod color scheme

Usage

```
scale_fill_dMod(...)
```

Arguments

...	arguments goint to codescale_color_manual()

stat.parlist *Gather statistics of a fitlist*

Description

Gather statistics of a fitlist

Usage

```
stat.parlist(x)
```

Arguments

x	The fitlist

steadyStates *Calculate analytical steady states.*

Description

This function follows the method published in [1]. The determined steady-state solution is tailored to parameter estimation. Please note that kinetic parameters might be fixed for solution of steady-state equations. Note that additional parameters might be introduced to ensure positivity of the solution.

The function calls a python script via rPython. Usage problems might occur when different python versions are used. The script was written and tested for python 2.7.12, sympy 0.7.6 and numpy 1.8.2.

Recently, users went into problems with RJSONIO when rPython was used. Unless a sound solution is available, please try to reinstall RJSONIO in these cases.

Usage

```
steadyStates(
  model,
  file = NULL,
  smatrix = NULL,
  states = NULL,
  rates = NULL,
  forcings = NULL,
  givenCQs = NULL,
  neglect = NULL,
  sparsifyLevel = 2,
  outputFormat = "R"
)
```

Arguments

model	Either name of the csv-file or the eqnlist of the model. If NULL, specify smatrix, states and rates by hand.
file	Name of the file to which the steady-state equations are saved. Read this file with readRDS.
smatrix	Numeric matrix, stiochiometry matrix of the system
states	Character vector, state vector of the system
rates	Character vector, flux vector of the system
forcings	Character vector with the names of the forcings
givenCQs	Character vector with conserved quantities. Use the format c("A + pA = totA", "B + pB = totB"). If NULL, conserved quantities are automatically calculated.
neglect	Character vector with names of states and parameters that must not be used for solving the steady-state equations
sparsifyLevel	numeric, Upper bound for length of linear combinations used for simplifying the stoichiometric matrix
outputFormat	Define the output format. By default "R" generating dMod compatible output. To obtain an output appropriate for d2d [2] "M" must be selected.

Value

Character vector of steady-state equations.

Author(s)

Marcus Rosenblatt, <marcus.rosenblatt@fdm.uni-freiburg.de>

References

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4863410/

[2] https://github.com/Data2Dynamics/d2d

Examples

```
## Not run:
reactions <- eqnlist()
reactions <- addReaction(reactions, "Tca_buffer", "Tca_cyto",
                         "import_Tca*Tca_buffer", "Basolateral uptake")
reactions <- addReaction(reactions, "Tca_cyto", "Tca_buffer",
                         "export_Tca_baso*Tca_cyto", "Basolateral efflux")
reactions <- addReaction(reactions, "Tca_cyto", "Tca_canalicular",
                         "export_Tca_cana*Tca_cyto", "Canalicular efflux")
reactions <- addReaction(reactions, "Tca_canalicular", "Tca_buffer",
                         "transport_Tca*Tca_canalicular", "Transport bile")

mysteadies <- steadyStates(reactions)
print(mysteadies)

## End(Not run)
```

strelide *Elide character vector*

Description

Elide character vector

Usage

```
strelide(string, width, where = "right", force = FALSE)
```

Arguments

string	String subject to eliding
width	Width including eliding ... of return string
where	Eliding can happen at 'left', 'middel', or 'right'. Defaults to 'right'.
force	Elide, even is <string> is shorter than <width>. Default to 'FALSE'.

Details

Elide a string to <width>. Eliding can happen at 'left', 'middle', or 'right'. #' If forcing = FALSE, which is the default, strings shorten than <width> are returend unaltered; forcing = TRUE inserts eliding symbols (...) in any case.

Value

Elided string of length <width>.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

strpad *Pad string to desired width*

Description

Pad string to desired width

Usage

```
strpad(string, width, where = "right", padding = " ", autoelide = FALSE)
```

Arguments

string	String to pad
width	Desired width of padded string
where	Padding can be inserted to the right or left of <string>. Default to 'right'.
padding	A single character with with the padding space is filled. Defaults to blank ' ' yielding invisible padding.
autoelide	If TRUE, <string> is elided if it is wider than <width>. The position of eliding follows <where>. Defaults to FALSE.

Value

Padded string of length <width>.

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

---

submatrix *Submatrix of a matrix returning ALWAYS a matrix*

Description

Submatrix of a matrix returning ALWAYS a matrix

Usage

```
submatrix(M, rows = 1:nrow(M), cols = 1:ncol(M))
```

Arguments

M	matrix
rows	Index vector
cols	Index vector

Value

The matrix `M[rows, cols]`, keeping/adjusting attributes like ncol nrow and dimnames.

subset.eqnlist *subset of an equation list*

Description

subset of an equation list

Usage

```
## S3 method for class 'eqnlist'
subset(x, ...)
```

Arguments

x	the equation list
...	logical expression for subsetting

Details

The argument ... can contain "Educt", "Product", "Rate" and "Description". The "

Value

An object of class eqnlist

Examples

```
reactions <- data.frame(Description = c("Activation", "Deactivation"),
                        Rate = c("act*A", "deact*pA"), A=c(-1,1), pA=c(1, -1) )
f <- as.eqnlist(reactions)
subset(f, "A" %in% Educt)
subset(f, "pA" %in% Product)
subset(f, grepl("act", Rate))
```

summary.eqnvec *Summary of an equation vector*

Description

Summary of an equation vector

Usage

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

Arguments

object	of class eqnvec.
...	additional arguments

Author(s)

Wolfgang Mader, <Wolfgang.Mader@fdm.uni-freiburg.de>

---

symmetryDetection *Search for symmetries in the loaded model*

Description

This function follows the method published in [1].

The function calls a python script via rPython. Usage problems might occur when different python versions are used. The script was written and tested for python 2.7.12, sympy 0.7.6.

Recently, users went into problems with RJSONIO when rPython was used. Unless a sound solution is available, please try to reinstall RJSONIO in these cases.

Usage

```
symmetryDetection(
  f,
  obsvect = NULL,
  prediction = NULL,
  initial = NULL,
  ansatz = "uni",
  pMax = 2,
  inputs = NULL,
  fixed = NULL,
  cores = 1,
  allTrafos = FALSE
)
```

Arguments

f	object containing the ODE for which as.eqnvec() is defined
obsvect	vector of observation functions
prediction	vector containing prediction to be tested
initial	vector containing initial values
ansatz	type of infinitesimal ansatz used for the analysis (uni, par, multi)
pMax	maximal degree of infinitesimal ansatz
inputs	specify the input variables
fixed	variables to concider fixed
cores	maximal number of cores used for the analysis
allTrafos	do not remove transformations with a common parameter factor

References

[1] https://journals.aps.org/pre/abstract/10.1103/PhysRevE.92.012920

Examples

```
## Not run:
eq <- NULL
eq <- addReaction(eq, "A", "B", "k1*A")
eq <- addReaction(eq, "B", "A", "k2*B")

observables <- eqnvec(Aobs = "alpha * A")

symmetryDetection(eq, observables)


## End(Not run)
```

---

theme_dMod *Standard plotting theme of dMod*

Description

Standard plotting theme of dMod

Usage

```
theme_dMod(base_size = 11, base_family = "")
```

Arguments

base_size	numeric, font-size
base_family	character, font-name

---

trust *Non-Linear Optimization*

Description

This function carries out a minimization or maximization of a function using a trust region algorithm. See the references for details.

Usage

```
trust(
  objfun,
  parinit,
  rinit,
  rmax,
  parscale,
  iterlim = 100,
  fterm = sqrt(.Machine$double.eps),
  mterm = sqrt(.Machine$double.eps),
  minimize = TRUE,
  blather = FALSE,
  parupper = Inf,
  parlower = -Inf,
  printIter = FALSE,
  ...
)

trustL1(
  objfun,
  parinit,
  mu = 0 * parinit,
  one.sided = FALSE,
  lambda = 1,
  rinit,
  rmax,
  parscale,
  iterlim = 100,
  fterm = sqrt(.Machine$double.eps),
  mterm = sqrt(.Machine$double.eps),
  minimize = TRUE,
  blather = FALSE,
  blather2 = FALSE,
  parupper = Inf,
  parlower = -Inf,
  printIter = FALSE,
  ...
)
```

Arguments

objfun	an R function that computes value, gradient, and Hessian of the function to be minimized or maximized and returns them as a list with components value, gradient, and hessian. Its first argument should be a vector of the length of parinit followed by any other arguments specified by the . . . argument.
parinit	starting parameter values for the optimization. Must be feasible (in the domain).
rinit	starting trust region radius. The trust region radius (see details below) is adjusted as the algorithm proceeds. A bad initial value wastes a few steps while the radius

	is adjusted, but does not keep the algorithm from working properly.
rmax	maximum allowed trust region radius. This may be set very large. If set small, the algorithm traces a steepest descent path (steepest ascent, when minimize = FALSE).
parscale	an estimate of the size of each parameter at the minimum. The algorithm operates as if optimizing function(x, ...) objfun(x / parscale, ...). May be missing in which case no rescaling is done. See also the details section below.
iterlim	a positive integer specifying the maximum number of iterations to be performed before the program is terminated.
fterm	a positive scalar giving the tolerance at which the difference in objective function values in a step is considered close enough to zero to terminate the algorithm.
mterm	a positive scalar giving the tolerance at which the two-term Taylor-series approximation to the difference in objective function values in a step is considered close enough to zero to terminate the algorithm.
minimize	If TRUE minimize. If FALSE maximize.
blather	If TRUE return extra info.
parupper	named numeric vector of upper bounds.
parlower	named numeric vector of lower bounds.
printIter	print iteration information to R console
...	additional argument to objfun
mu	named numeric value. The reference value for L1 penalized parameters.
one.sided	logical. One-sided penalization.
lambda	strength of the L1 penalty
blather2	even more information

Details

See Fletcher (1987, Section 5.1) or Nocedal and Wright (1999, Section 4.2) for detailed expositions.

Value

A list containing the following components:

- value: the value returned by objfun at the final iterate.
- gradient: the gradient returned by objfun at the final iterate.
- hessian: the Hessian returned by objfun at the final iterate.
- argument: the final iterate
- converged: if TRUE the final iterate was deemed optimal by the specified termination criteria.
- iterations: number of trust region subproblems done (including those whose solutions are not accepted).
- argpath: (if blather == TRUE) the sequence of iterates, not including the final iterate.
- argtry: (if blather == TRUE) the sequence of solutions of the trust region subproblem.

- steptype: (if blather == TRUE) the sequence of cases that arise in solutions of the trust region subproblem. "Newton" means the Newton step solves the subproblem (lies within the trust region). Other values mean the subproblem solution is constrained. "easy-easy" means the eigenvectors corresponding to the minimal eigenvalue of the rescaled Hessian are not all orthogonal to the gradient. The other cases are rarely seen. "hard-hard" means the Lagrange multiplier for the trust region constraint is minus the minimal eigenvalue of the rescaled Hessian; "hard-easy" means it isn't.
- accept: (if blather == TRUE) indicates which of the sequence of solutions of the trust region subproblem were accepted as the next iterate. (When not accepted the trust region radius is reduced, and the previous iterate is kept.)
- r: (if blather == TRUE) the sequence of trust region radii.
- rho: (if blather == TRUE) the sequence of ratios of actual over predicted decrease in the objective function in the trust region subproblem, where predicted means the predicted decrease in the two-term Taylor series model used in the subproblem.
- valpath: (if blather == TRUE) the sequence of objective function values at the iterates.
- valtry: (if blather == TRUE) the sequence of objective function values at the solutions of the trust region subproblem.
- preddiff: (if blather == TRUE) the sequence of predicted differences using the two-term Taylor-series model between the function values at the current iterate and at the solution of the trust region subproblem.
- stepnorm: (if blather == TRUE) the sequence of norms of steps, that is distance between current iterate and proposed new iterate found in the trust region subproblem.

`unique.parframe` *Extract those lines of a parameter frame with unique elements in the value column*

Description

Extract those lines of a parameter frame with unique elements in the value column

Usage

```
## S3 method for class 'parframe'
unique(x, incomparables = FALSE, tol = 1, ...)
```

Arguments

`x`	parameter frame
`incomparables`	not used. Argument exists for compatibility with S3 generic.
`tol`	tolerance to decide when values are assumed to be equal, see `plotValues()`.
`...`	additional arguments being passed to `plotValues()`, e.g. for subsetting.

Value

A subset of the parameter frame `x`.

wide2long *Translate wide output format (e.g. from ode) into long format*

Description

Translate wide output format (e.g. from ode) into long format

Usage

```
wide2long(out, keep = 1, na.rm = FALSE)
```

Arguments

out	data.frame or matrix or list of matrices in wide format
keep	Index vector, the columns to keep
na.rm	Logical, if TRUE, missing values are removed in the long format.

Details

The function assumes that out[,1] represents a time-like vector whereas out[,-1] represents the values. Useful for plotting with ggplot. If a list is supplied, the names of the list are added as extra column names "condition"

Value

data.frame in long format, i.e. columns "time" (out[,1]), "name" (colnames(out[,-1])), "value" (out[,-1]) and, if out was a list, "condition" (names(out))

wide2long.data.frame *Translate wide output format (e.g. from ode) into long format*

Description

Translate wide output format (e.g. from ode) into long format

Usage

```
## S3 method for class 'data.frame'
wide2long(out, keep = 1, na.rm = FALSE)
```

Arguments

out	data.frame or matrix or list of matrices in wide format
keep	Index vector, the columns to keep
na.rm	Logical, if TRUE, missing values are removed in the long format.

Details

The function assumes that out[,1] represents a time-like vector whereas out[,-1] represents the values. Useful for plotting with ggplot. If a list is supplied, the names of the list are added as extra column names "condition"

Value

data.frame in long format, i.e. columns "time" (out[,1]), "name" (colnames(out[,-1])), "value" (out[,-1]) and, if out was a list, "condition" (names(out))

`wide2long.list` *Translate wide output format (e.g. from ode) into long format*

Description

Translate wide output format (e.g. from ode) into long format

Usage

```
## S3 method for class 'list'
wide2long(out, keep = 1, na.rm = FALSE)
```

Arguments

`out`	list of matrices in wide format
`keep`	Index vector, the columns to keep
`na.rm`	Logical, if `TRUE`, missing values are removed in the long format.

Details

The function assumes that out[,1] represents a time-like vector whereas out[,-1] represents the values. Useful for plotting with ggplot. If a list is supplied, the names of the list are added as extra column names "condition"

Value

data.frame in long format, i.e. columns "time" (out[,1]), "name" (colnames(out[,-1])), "value" (out[,-1]) and, if out was a list, "condition" (names(out))

wide2long.matrix *Translate wide output format (e.g. from ode) into long format*

Description

Translate wide output format (e.g. from ode) into long format

Usage

```
## S3 method for class 'matrix'
wide2long(out, keep = 1, na.rm = FALSE)
```

Arguments

out	data.frame or matrix or list of matrices in wide format
keep	Index vector, the columns to keep
na.rm	Logical, if TRUE, missing values are removed in the long format.

Details

The function assumes that out[,1] represents a time-like vector whereas out[,-1] represents the values. Useful for plotting with ggplot. If a list is supplied, the names of the list are added as extra column names "condition"

Value

data.frame in long format, i.e. columns "time" (out[,1]), "name" (colnames(out[,-1])), "value" (out[,-1]) and, if out was a list, "condition" (names(out))

write.eqnlist *Write equation list into a csv file*

Description

Write equation list into a csv file

Usage

```
write.eqnlist(eqnlist, ...)
```

Arguments

eqnlist	object of class eqnlist
...	Arguments going to write.table

wrss *Compute the weighted residual sum of squares*

Description

Compute the weighted residual sum of squares

Usage

```
wrss(nout)
```

Arguments

nout	data.frame (result of res) or object of class objframe.

Value

list with entries value (numeric, the weighted residual sum of squares), gradient (numeric, gradient) and hessian (matrix of type numeric).

Xd *Model prediction function from data.frame*

Description

Model prediction function from data.frame

Usage

```
Xd(data, condition = NULL)
```

Arguments

data	data.frame with columns "name", "time", and row names that are taken as parameter names. The data frame can contain a column "value" to initialize the parameters.
condition	either NULL (generic prediction for any condition) or a character, denoting the condition for which the function makes a prediction.

Value

Object of class prdfn, i.e. a function `x(times pars, deriv = TRUE, conditions = NULL)`, see also Xs. Attributes are "parameters", the parameter names (row names of the data frame), and possibly "pouter", a named numeric vector which is generated from `data$value`.

Examples

```
# Generate a data.frame and corresponding prediction function
timesD <- seq(0, 2*pi, 0.5)
mydata <- data.frame(name = "A", time = timesD, value = sin(timesD),
                     row.names = paste0("par", 1:length(timesD)))
x <- Xd(mydata)

# Evaluate the prediction function at different time points
times <- seq(0, 2*pi, 0.01)
pouter <- structure(mydata$value, names = rownames(mydata))
prediction <- x(times, pouter)
plot(prediction)
```

`Xf` *Model prediction function for ODE models without sensitivities.*

Description

Interface to get an ODE into a model function `x(times, pars, forcings, events)` returning ODE output. It is a reduced version of Xs, missing the sensitivities.

Usage

```
Xf(
  odemodel,
  forcings = NULL,
  events = NULL,
  condition = NULL,
  optionsOde = list(method = "lsoda")
)
```

Arguments

`odemodel`	Object of class odemodel.
`forcings,`	see Xs
`events,`	see Xs
`condition`	either NULL (generic prediction for any condition) or a character, denoting the condition for which the function makes a prediction.
`optionsOde`	list with arguments to be passed to odeC() for the ODE integration.

Details

Can be used to integrate additional quantities, e.g. fluxes, by adding them to `f`. All quantities that are not initialised by pars in `x(..., forcings, events)` are initialized with 0. For more details and the return value see Xs.

Xs *Model prediction function for ODE models.*

Description

Interface to combine an ODE and its sensitivity equations into one model function `x(times, pars, deriv = TRUE)` returning ODE output and sensitivities.

Usage

```
Xs(
  odemodel,
  forcings = NULL,
  events = NULL,
  names = NULL,
  condition = NULL,
  optionsOde = list(method = "lsoda"),
  optionsSens = list(method = "lsodes")
)
```

Arguments

odemodel	object of class odemodel
forcings	data.frame with columns name (factor), time (numeric) and value (numeric). The ODE forcings.
events	data.frame of events with columns "var" (character, the name of the state to be affected), "time" (numeric, time point), "value" (numeric, value), "method" (character, either "replace", "add" or "multiply"). See events. ATTENTION: Sensitivities for event states will only be correctly computed if defined within odemodel(). Specify events within Xs() only for forward simulation.
names	character vector with the states to be returned. If NULL, all states are returned.
condition	either NULL (generic prediction for any condition) or a character, denoting the condition for which the function makes a prediction.
optionsOde	list with arguments to be passed to odeC() for the ODE integration.
optionsSens	list with arguments to be passed to odeC() for integration of the extended system

Value

Object of class prdfn. If the function is called with parameters that result from a parameter transformation (see P), the Jacobian of the parameter transformation and the sensitivities of the ODE are multiplied according to the chain rule for differentiation. The result is saved in the attributed "deriv", i.e. in this case the attibutes "deriv" and "sensitivities" do not coincide.

Xt *Generate a prediction function that returns times*

Description

Function to deal with non-ODE models within the framework of dMod. See example.

Usage

```
Xt(condition = NULL)
```

Arguments

condition	either NULL (generic prediction for any condition) or a character, denoting the condition for which the function makes a prediction.

Value

Object of class prdfn.

Examples

```
x <- Xt()
g <- Y(c(y = "a*time^2+b"), f = NULL, parameters = c("a", "b"))

times <- seq(-1, 1, by = .05)
pars <- c(a = .1, b = 1)

plot((g*x)(times, pars))
```

Y *Observation functions.*

Description

Creates an object of type obsfn that evaluates an observation function and its derivatives based on the output of a model prediction function, see prdfn, as e.g. produced by Xs.

Usage

```
Y(
  g,
  f = NULL,
  states = NULL,
  parameters = NULL,
  condition = NULL,
```

```
  attach.input = TRUE,
  deriv = TRUE,
  compile = FALSE,
  modelname = NULL,
  verbose = FALSE
)
```

Arguments

g	Named character vector or equation vector defining the observation function
f	Named character of equations or object that can be converted to eqnvec or object of class fn. If f is provided, states and parameters are guessed from f.
states	character vector, alternative definition of "states", usually the names of f. If both, f and states are provided, the states argument overwrites the states derived from f.
parameters	character vector, alternative definition of the "parameters", usually the symbols contained in "g" and "f" except for states and the code word time. If both, f and parameters are provided, the parameters argument overwrites the parameters derived from f and g.
condition	either NULL (generic prediction for any condition) or a character, denoting the condition for which the function makes a prediction.
attach.input	logical, indiating whether the original input should be returned with the output.
deriv	logical, generate function to evaluate derivatives of observables. Necessary for parameter estimation.
compile	Logical, compile the function (see funC0)
modelname	Character, used if compile = TRUE, sets a fixed filename for the C file.
verbose	Print compiler output to R command line.

Details

For odemodels with forcings, it is best, to pass the prediction function x to the "f"-argument instead of the equations themselves. If an eqnvec is passed to "f" in this case, the forcings and states have to be specified manually via the "states"-argument.

Value

Object of class obsfn, i.e. a function y(..., deriv = TRUE, conditions = NULL) representing the evaluation of the observation function. Arguments out (model prediction) and pars (parameter values) shoudl be passed by the ... argument. If out has the attribute "sensitivities", the result of y(out, pars), will have an attributed "deriv" which reflecs the sensitivities of the observation with respect to the parameters. If pars is the result of a parameter transformation p(pars) (see P), the Jacobian of the parameter transformation and the sensitivities of the observation function are multiplied according to the chain rule for differentiation.

Examples

```
# Define a time grid on which to make a prediction by peace-wise linear function.
# Then define a (generic) prediction function based on thid grid.
times <- 0:5
grid <- data.frame(name = "A", time = times, row.names = paste0("p", times))
x <- Xd(grid)

# Define an observable and an observation function
observables <- eqnvec(Aobs = "s*A")
g <- Y(g = observables, f = NULL, states = "A", parameters = "s")

# Collect parameters and define an overarching parameter transformation
# for two "experimental condtions".
dynpars <- attr(x, "parameters")
obspars <- attr(g, "parameters")
innerpars <- c(dynpars, obspars)

trafo <- structure(innerpars, names = innerpars)
trafo_C1 <- replaceSymbols(innerpars, paste(innerpars, "C1", sep = "_"), trafo)
trafo_C2 <- replaceSymbols(innerpars, paste(innerpars, "C2", sep = "_"), trafo)

p <- NULL
p <- p + P(trafo = trafo_C1, condition = "C1")
p <- p + P(trafo = trafo_C2, condition = "C2")

# Collect outer (overarching) parameters and
# initialize with random values
outerpars <- attr(p, "parameters")
pars <- structure(runif(length(outerpars), 0, 1), names = outerpars)

# Predict internal/unobserved states
out1 <- (x*p)(times, pars)
plot(out1)

# Predict observed states in addition to unobserved
out2 <- (g*x*p)(times, pars)
plot(out2)
```

`%.*%` *Multiplication of objective functions with scalars*

Description

The `%.*%` operator allows to multiply objects of class objlist or objfn with a scalar.

Usage

```
x1 %.*% x2
```

Arguments

x1	object of class objfn or objlist.
x2	numeric of length one.

Value

An objective function or objlist object.

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