Package ‘cellGrowth’

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Maintainer Julien Gagneur <`gagneur@genzentrum.lmu.de`>

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Title Fitting cell population growth models

Author Julien Gagneur <`gagneur@genzentrum.lmu.de`>, Andreas Neudecker <`a.neudecker@arcor.de`>

Description This package provides functionalities for the fitting of cell population growth models on experimental OD curves.

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`bandwidthCV` *Bandwidth cross-validation*

Description

Perform cross-validation to detect optimal bandwidth

Usage

```
bandwidthCV(well, fileParser = readYeastGrower,
  getWellIds = getWellIdsTecan,
  bandwidths = seq(0.5 * 3600, 10 * 3600, length.out = 30),
  nFold = 10, nWell = 100, cutoff = 0.95,
  calibration = identity, scaleY = log2)
```

Arguments

`well`	well dataframe. See `wellDataFrame`.
`fileParser`	Converts the file generated by the machine to proper R format. See `readYeastGrower` for details.
`getWellIds`	function or vector. If function its parameter is the return value of fileParser. It should return a vector containing the well ids (e.g. A01, A02, ...). You can set the well ids vector directly. See `getWellIdsTecan`.
`bandwidths`	vector of bandwidths to test on
`nFold`	`integer`. In how many parts is the sample divided for cross-validation?
`nWell`	`integer`. How many wells out of the well dataframe will be used for cross validation?
`cutoff`	`scalar` between 0 and 1. See details.
`calibration`	`function` or `list of functions`. If function, calibration is applied to all raw data. If list, the well dataframe must contain a column `machine`. Depending on that column the according function in the list is applied to the raw data. See details
`scaleY`	`function` applied to the calibrated data.

Details

This function needs a few minutes time. The "optimal" bandwidth is the largest bandwidth which is in 95% (cutoff parameter) of all cases within one standard deviation of the best bandwidth. This should make the derivative of the fitted curve more robust. The raw values from the machine might not be directly optical densities (OD), which is needed to infer doubling time. Calibration functions for each machine can be provided to map raw values into OD using the `calibration` parameter.

Value

list with entries

`bandwidth`	"optimal" bandwidth
`well`	well dataframe
`bandwidths`	tested bandwidths
`err2`	squared error
`err2std`	Standard deviation of squared error
`muStd`	Standard deviation of max growth rate
`oneStdOfMini`	bandwidths within one std of best

Author(s)

Julien Gagneur and Andreas Neudecker

Examples

```
folder <- system.file("extdata", package="cellGrowth")
well <- wellDataFrame(file.path(folder, "plateLayout.txt"), file.path(folder,"machineRun.txt"))

## for a fast example, we use nWell = 1 here. Use a large number (default 100) for real life applications
bw <- bandwidthCV(well, nWell=1)
```

`baranyi` *Baranyi growth model*

Description

Baranyi growth model as defined in Kelly et al.

Usage

```
baranyi(x, mu, l, z0, zmax)
```

Arguments

`x`	`numeric` vector: time points for which log(OD) must be computed
`mu`	`numeric` scalar: maximal growth rate parameter
`l`	`numeric` scalar: time lag parameter
`z0`	`numeric` scalar: minimal log(OD) parameter
`zmax`	`numeric` scalar: maximal log(OD) parameter

Value

`numeric` vector: log(OD) for the time points given in `x`

Author(s)

Julien Gagneur

References

Kelly et al., The use of dummy data points when fitting bacterial growth curves, IMA Journal of Mathematics Applied in Medicine and Biology (1999) 16, 155-170

Examples

```
x = 1:1000
y = baranyi(x, mu=0.01, l=200, z0=1, zmax=5)
plot(x,y)
```

`fitCellGrowth` *Fit growth curves*

Description

Fit a cell growth curve

Usage

```
fitCellGrowth(x, z, model = "locfit",
  locfit.h = 3 * 60 * 60, locfit.deg = 2,
  relative.height.at.lag = 0.1)
```

Arguments

`x`	`numeric` vector: time points
`z`	`numeric` vector: log(OD)
`model`	which model to fit.
`locfit.h`	`numeric`: `h` parameter (window size) in call to `locfit`. The default value is set to three hours assuming `x` given in seconds. You can detect a better bandwidth by calling `bandwidthCV`
`locfit.deg`	`numeric`: `deg` parameter (polynomials degree) in call to `locfit`
`relative.height.at.lag`	Parameter used by `guessCellGrowthParams`

Details

For the non-parametric "locfit" model, local regression is done by a call to `locfit`. The returned maximum growth rate values the maximum value of the fitted derivative over the data points. For the parametric models "logistic", "gompertz", "rosso" and "baranyi", the function does a non-least square fit by calling `nls`. Initial parameters values are generated by `guessCellGrowthParams`. The returned maximum growth rate values the `mu` parameter of these models.

Value

Fit as returned by `locfit` for the "locfit" model and as returned by `nls` for the "logistic", "gompertz", "rosso" and "baranyi" models. The returned value also has an attribute `maxGrowthRate` valueing the inferred maximum growth rate as well as an attribute `pointOfMaxGrowthRate` valuing the datapoint at which the growth rate is maximal. Also, it has an attribute `max` valuing the inferred maximum among the time points as well as `pointOfMax` valuing the datapoint of max fitted value. It gets the additional class `cellCurveFit` assigned.

Author(s)

Julien Gagneur and Moritz Matthey

See Also

`nls`, `locfit`, `baranyi`, `gompertz`, `logistic`, `rosso`, `guessCellGrowthParams`, `fitCellGrowths`

Examples

```
x = 1:1000
          z = gompertz(x, mu=0.01, l=200, z0=1, zmax=5) + rnorm(length(x),sd=0.1)
          f = fitCellGrowth(x, z, model = "gompertz")
          floc = fitCellGrowth(x, z, model = "locfit", locfit.h=500)
           plot(x,z, main="simulated data\nGompertz model")
           lines(x, predict(f,x), lwd=2, col="red")
           lines(x, predict(floc,x), lwd=2, col="blue")
         legend( "right", legend=c("gompertz fit", "locfit"), lwd=1, col=c("red","blue") )
```

`fitCellGrowths` *Fit multiple growth curves*

Description

Fit growth curves for multiple wells

Usage

```
fitCellGrowths(well, plot.folder = NULL,
  model = "locfit", xlab = "time",
  ylab = expression(log2(Absorption)), scaleX = 1,
  scaleY = log2, calibration = identity,
  fileParser = readYeastGrower,
  getWellIds = getWellIdsTecan, locfit.h = 3 * 60 * 60,
  bandwidths = seq(0.5 * 3600, 10 * 3600, length.out = 30),
  nFold = 10, nWell = 100, cutoff = 0.95, ...)
```

Arguments

`well`	data.frame with mandatory columns directory, filename, well. See `wellDataFrame`
`plot.folder`	see details
`model`	model to choose for fitting growth curve
`fileParser`	Converts the file generated by the machine to proper R format. See `readYeastGrower` for details.
`xlab`	plot parameter
`ylab`	plot parameter
`scaleX`	useful if you want to get the doubling in another unit, e.g. days instead of seconds.
`scaleY`	`function` applied to the calibrated data.
`calibration`	`function` or `list` of `functions`. If function, calibration is applied to all raw data. If list, the well dataframe must contain a column `machine`. Depending on that column the according function in the list is applied to the raw data. See details
`getWellIds`	function or vector. If function its parameter is the return value of fileParser. It should return a vector containing the well ids (e.g. A01, A02, ...). You can set the well ids vector directly. See `getWellIdsTecan`.
`locfit.h`	bandwidth parameter for local polynomial fitting. If set to "bandwidthCV" bandwidth is automatically selected through `bandwidthCV`
`bandwidths`	passed to `bandwidthCV` if locfit.h="bandwidthCV"
`nFold`	passed to `bandwidthCV` if locfit.h="bandwidthCV"
`nWell`	passed to `bandwidthCV` if locfit.h="bandwidthCV"
`cutoff`	passed to `bandwidthCV` if locfit.h="bandwidthCV"
`...`	Parameter is passed to `fitCellGrowth`

Details

Essentially a wrapper for `fitCellGrowth`. The function gets a well object and fits a growth curve on all wells. It computes the doubling frequency observed in a well and extracts the maximal growth rate (1/minimal doubling time). The raw values from the machine might not be directly optical densities (OD), which is needed to infer doubling time. Calibration functions for each machine can be provided to map raw values into OD using the `calibration` parameter. If the parameter plot.folder is set, the function creates a folder within plot.folder for each file in the well object. For each well a plot is written into that folder, named `well_id.png`.

Value

dataframe with entries

`maxGrowthRate`	maximal growth rate
`pointOfMaxGrowthRate`	datapoint where growth rate is maximal
`max`	inferred maximum among the time points
`pointOfMax`	datapoint of the max fitted value

Author(s)

Julien Gagneur and Andreas Neudecker

See Also

`fitCellGrowth`

Examples

```
plateLayout <- system.file("extdata", "plateLayout.txt", package="cellGrowth")
machineRun <- system.file("extdata", "machineRun.txt", package="cellGrowth")
well <- wellDataFrame(plateLayout,machineRun)
cal <- function(x){x+1}
fit <- fitCellGrowths(well,plot.folder="data",calibration=cal)
```

`getRowColumn` *Convert well ids to row and column*

Description

Converts well ids to row and column

Usage

```
getRowColumn(wellId)
```

Arguments

`wellId`	vector of well ids

Value

vector of lists containing row and column

Author(s)

Andreas Neudecker

Examples

```
getRowColumn(c("A01","B05"))
```

`getWellIdsTecan` *Get aliases for wells*

Description

The aliases are generated by extracting the information from parsed data of the file generated by the tecan machine. See `readYeastGrower` and `readGenios`.

Usage

```
getWellIdsTecan(data)
```

Arguments

`data`	parsed data of the file. See `readYeastGrower` and `readGenios`

Value

vector containing the aliases

Author(s)

Julien Gagneur, Andreas Neudecker

Examples

```
data <- readYeastGrower( system.file("extdata", "Plate1_YPFruc.txt", package="cellGrowth"))
ids <- getWellIdsTecan(data)
```

`gompertz` *Gompertz growth model*

Description

Gompertz growth model as defined in Zwietering et al.

Usage

```
gompertz(x, mu, l, z0, zmax)
```

Arguments

`x`	`numeric` vector: time points for which log(OD) must be computed
`mu`	`numeric` scalar: maximal growth rate parameter
`l`	`numeric` scalar: time lag parameter
`z0`	`numeric` scalar: minimal log(OD) parameter
`zmax`	`numeric` scalar: maximal log(OD) parameter

Value

`numeric` vector: log(OD) for the time points given in `x`

Author(s)

Julien Gagneur

References

Zwietering, et al. Modeling of the Bacterial Growth Curve, APPLIED AND ENVIRONMENTAL MICROBIOLOGY, 1990.

Examples

```
x = 1:1000
y = gompertz(x, mu=0.01, l=200, z0=1, zmax=5)
plot(x,y)
```

`guessCellGrowthParams` *Guess growth models parameters*

Description

Guess initial parameters values for growth models

Usage

```
guessCellGrowthParams(x, z, relative.height.at.lag = 0.1)
```

Arguments

`x`	`numeric` vector: time points
`z`	codenumeric vector: log(OD)
`relative.height.at.lag`	`numeric` scalar (see Details)

Details

The relative.height.at.lag parameter should be close to the relative height of the point, where the curve reaches its maximal slope. If the fitting fails, try to set this parameter to a different value.

Value

A list with entries:

`mu`	`numeric` scalar: maximal growth rate parameter
`l`	`numeric` scalar: time lag parameter
`z0`	`numeric` scalar: minimal log(OD) parameter
`zmax`	`numeric` scalar: maximal log(OD) parameter

Author(s)

Julien Gagneur

Examples

```
x <- 1:1000
z <- gompertz(x, mu=0.01, l=200, z0=1, zmax=5)+rnorm(length(x),mean=0,sd=0.25)
guess <- guessCellGrowthParams(x,z,relative.height.at.lag=0.5)
fit <- nls(z~gompertz(x,mu,l,z0,zmax),start=guess)
plot(x,z)
lines(x,predict(fit,x),lwd=2,col=”red”)
```

`logistic` *Logistic growth model*

Description

Logistic growth model as defined in Zwietering et al.

Usage

```
logistic(x, mu, l, z0, zmax)
```

Arguments

`x`	`numeric` vector: time points for which log(OD) must be computed
`mu`	`numeric` scalar: maximal growth rate parameter
`l`	`numeric` scalar: time lag parameter
`z0`	`numeric` scalar: minimal log(OD) parameter
`zmax`	`numeric` scalar: maximal log(OD) parameter

Value

`numeric` vector: log(OD) for the time points given in `x`

Author(s)

Julien Gagneur

References

Zwietering, et al. Modeling of the Bacterial Growth Curve, APPLIED AND ENVIRONMENTAL MICROBIOLOGY, 1990.

Examples

```
x = 1:1000
y = logistic(x, mu=0.01, l=200, z0=1, zmax=5)
plot(x,y)
```

`plot.cellGrowthFit` *Generic plot function for datatype cellGrowthFit*

Description

Plot of a growth curve showing raw data and fitted curve

Usage

```
plot.cellGrowthFit(x, scaleX = 1, xlab = "time",
  ylab = "log2(OD)", lwd = 0.5, ...)
```

Arguments

`x`	growth curve object. See `fitCellGrowth`
`scaleX`	scalar affecting the scaling of the x-axis.
`xlab`	plot parameter
`ylab`	plot parameter
`lwd`	plot parameter
`...`	optional plot parameters passed to the plot function

Author(s)

Andreas Neudecker

Examples

```
# Parse file
dat = readYeastGrower( system.file("extdata", "Plate1_YPFruc.txt", package="cellGrowth") )

# fit
n <- names( dat$OD)[36]
fit <- fitCellGrowth(x=dat$time,z=log2(dat$OD[[n]]), model = "locfit")
plot(fit)
```

`plot.well` *Generic plot function for datatype well*

Description

Plots well plate as lattice xyplot.

Usage

```
plot.well(x, file = NULL, labelColumn = NULL,
  calibration = identity, ...)
```

Arguments

`x`	the well object
`file`	which plate file to plot? If NULL (default) the first file is taken.
`labelColumn`	column in the well object to take label for the wells from
`calibration`	`function` or `list` of `functions`. If calibration is a function it is applied to all raw data. If it is a list, the well dataframe must contain a column named `machine`. Depending on that column the according function in the list is applied to the raw data.
`...`	optional plot parameters, see details

Details

This function calls `plotPlate` for the plate `plate`. The ... parameter is passed to the `plotPlate` function.

Author(s)

Andreas Neudecker

`plotPlate` *Plot of a well plate*

Description

Plot of a well plate directly from a file using a lattice xyplot

Usage

```
plotPlate(file, labels = NULL,
  fileParser = readYeastGrower,
  getWellIds = getWellIdsTecan, calibration = identity,
  extractRowColumn = getRowColumn, cex = 0.05,
  scaleX = 1, scaleY = log2, strip.lines = 1.05,
  strip.cex = 0.8, xlab = "time", ylab = "log2(OD)",
  main = basename(file),
  scales = list(x = list(rot = 45)), ...)
```

Arguments

`file`	file name
`labels`	`vector` of characters indicating the label of the wells
`fileParser`	the file parser which reads the file generated by the machine
`getWellIds`	function or vector. If getWellIds is a function its parameter is the parsed data of the file parsed by `fileParser`. It should return a vector containing the well identifiers, e.g. A01, A02, .. You can as well set the well identifiers as a vector directly

`calibration`	calibration function applied to the raw data (before scaleY is applied)
`extractRowColumn`	function which converts well identifiers into row and column names
`cex`	plot parameter
`scaleX`	factor which scales the x-axis
`scaleY`	function how to convert the y-axis (e.g. log2)
`strip.lines`	height in lines of the labels
`strip.cex`	text-size of the labels
`xlab`	plot parameter
`ylab`	plot parameter
`main`	plot parameter
`scales`	plot parameter
`...`	optional plot parameter. See details

Details

All plot parameters are passed to the `xyplot` function

Author(s)

Andreas Neudecker

Examples

```
plotPlate( system.file("extdata", "tecan_genios.txt", package="cellGrowth"), fileParser=readGenios)
```

`readGenios` *Read Tecan Genios data files*

Description

Read raw data file form Tecan Genios instrument

Usage

```
readGenios(file)
```

Arguments

`file`	filename

Value

a list with entries:

`time`	a `numeric` vector of time points
`OD`	a `data.frame` vector of measured OD. The colnames are the well names.
`read`	a `numeric` vector of read numbers
`temperature`	a `numeric` vector of temperatures
`header`	a `character` vector: the header of the file

Author(s)

Julien Gagneur

See Also

`readYeastGrower`

Examples

```
# Get file names
# Parse file
dat = readGenios( system.file("extdata", "tecan_genios.txt", package="cellGrowth") )

# fit
n <- names( dat$OD)[36]
fit <- fitCellGrowth(x=dat$time,z=log2(dat$OD[[n]]), model = "locfit",locfit.h=6*60*60)
plot(fit)
```

`readYeastGrower` *Read Yeast Grower data files*

Description

Read raw data file from Yeast Grower software

Usage

```
readYeastGrower(file)
```

Arguments

`file`	filename

Value

a list with entries:

`time`	a `numeric` vector of time points
`OD`	a `data.frame` vector of measured OD. The colnames are the well names.
`read`	a `numeric` vector of read numbers
`temperature`	a `numeric` vector of temperatures
`header`	a `character` vector: the header of the file

Author(s)

Julien Gagneur

See Also

`readGenios`

Examples

```
# Get file names
# Parse file
dat = readYeastGrower( system.file("extdata", "Plate1_YPFruc.txt", package="cellGrowth") )

# fit
n <- names( dat$OD)[36]
fit <- fitCellGrowth(x=dat$time,z=log2(dat$OD[[n]]), model = "locfit")
plot(fit)
```

`rosso` *Rosso growth model*

Description

Rosso growth model

Usage

```
rosso(x, mu, l, z0, zmax)
```

Arguments

`x`	vector: time points for which log(OD) must be computed
`mu`	scalar: maximal growth rate parameter
`l`	scalar: time lag parameter
`z0`	scalar: minimal log(OD) parameter
`zmax`	scalar: maximal log(OD) parameter

Details

Rosso model is z0 if x<=l zmax - log(1 + (exp(zmax-z0) -1)*exp(-mu*(x-l))) otherwise

Value

vector: log(OD) for the time points given in `x`

Author(s)

Julien Gagneur

Examples

```
x = 1:1000
y = rosso(x, mu=0.01, l=200, z0=1, zmax=5)
plot(x,y)
```

`standardWellId` *Make standard names for well ids*

Description

Make standard names for well in 96 well plates

Usage

```
standardWellId(wellId)
```

Arguments

`wellId`	vector of well ids

Details

A1 -> A01 A01 -> A01

Value

standard well name

Author(s)

Julien Gagneur

Examples

```
standardWellId( c("A1", "B01", "H2"))
```

`wellDataFrame` *Create a well data frame*

Description

Load a plate layout file and a file specifying the machine runs

Usage

```
wellDataFrame(plateLayoutFile, machineRunFile)
```

Arguments

`plateLayoutFile`	a file containing the plate layout. The file must contain a column named `plate` and a column named `well`
`machineRunFile`	a file containing the machine runs The file must contain columns named `directory`, `filename` and `plate` specifying the directory and filename of the data for the corresponding run. The column `use` is optional. If present, only rows with `use == TRUE` are put into the dataframe.

Details

See the provided example files for the layout and machine run file formats.

Value

an object of class well and data.frame

Author(s)

Andreas Neudecker

Examples

```
plateLayout <-  system.file("extdata", "plateLayout.txt", package="cellGrowth")
machineRun <-  system.file("extdata", "machineRun.txt", package="cellGrowth")
well <- wellDataFrame(plateLayout,machineRun)
plot(well,plate=1)
```

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