Package 'cellVolumeDist'

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Type Package

Title Functions to Fit Cell Volume Distributions and Thereby Estimate
Cell Growth Rates and Division Times

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Depends minpack.lm (>= 1.1-1), gplots

Description Implements a methodology for using cell volume
distributions to estimate cell growth rates and division times
that is described in the paper entitled, ``Cell Volume
Distributions Reveal Cell Growth Rates and Division Times'', by
Michael Halter, John T. Elliott, Joseph B. Hubbard, Alessandro
Tona and Anne L. Plant, which is in press in the Journal of
Theoretical Biology. In order to reproduce the analysis used
to obtain Table 1 in the paper, execute the command
``example(fitVolDist)''.

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cellVolumeDist-package

Functions to fit cell volume distributions and thereby estimate cell growth rates and division times

Description

This package implements a methodology for using cell volume distributions to estimate cell growth rates and division times that is described in the paper entitled "Cell Volume Distributions Reveal Cell Growth Rates and Division Times", by Michael Halter, John T. Elliott, Joseph B. Hubbard, Alessandro Tona and Anne L. Plant, which is in press in the Journal of Theoretical Biology. In order to reproduce the analysis used to obtain Table 1 in the paper, execute the command example(fitVolDist).

Details

The package fits a model for cell volume distributions under least squares criteria using the function nls.lm. Estimates for cell growth rate and division time are thereby obtained.

References

Halter M, Elliott JT, Hubbard JB, Tona A, Plant AL (2009), "Cell Volume Distributions Reveal Cell Growth Rates and Division Times", Journal of Theoretical Biology, Vol 257, pp 124 - 130, DOI: 10.1016/j.jtbi.2008.10.031.

See Also

nls.lm

A10_vSMC_volume_data   *Volume distribution data for A10 vSMC cell cultures*

Description

Volume distribution data for A10 vSMC cell cultures with the DNA polymerase inhibitor aphidicolin added at 0nM, 50nM and 100nM concentration.

Usage

data(A10_vSMC_volume_data)

Format

The data is formated as 12 numeric vectors of length 257 representing cell volume (μm^3) distributions, namely "Aph0_a", "Aph0_b", "Aph0_c", "Aph0_d", "Aph50_a", "Aph50_b", "Aph50_c", "Aph50_d", "Aph100_a", "Aph100_b", "Aph100_c", and "Aph100_d". The name of the object indicates the concentration of aphidicolin present in nM (e.g., "Aph0_a" represents measurements in the presence of 0nM of aphidicolin). Four repetitions of measurements at each of the three concentrations are included.

The estimated cell cycle time (h) for each volume distribution dataset is indicated in the numeric objects "tAph0_a", "tAph0_b", "tAph0_c", "tAph0_d", "tAph50_a", "tAph50_b", "tAph50_c", "tAph50_d", "tAph100_a", "tAph100_b", "tAph100_c", and "tAph100_d".

The object "volumes_A10_vSMC" is a numeric vector representing the volumes (μm^3) associated with all of the distributions.

Source

The measurement protocol is described in the paper in the references.

References

Halter M, Elliott JT, Hubbard JB, Tona A, Plant AL (2009), "Cell Volume Distributions Reveal Cell Growth Rates and Division Times", Journal of Theoretical Biology, Vol 257, pp 124 - 130, DOI: 10.1016/j.jtbi.2008.10.031.

Examples

```
data(A10_vSMC_volume_data)
plot(volumes_A10_vSMC, Aph100_b,
main=expression(paste("Distribution of cell volumes (",mu, m^3,")",sep="")),
type="b", pch=20, ylab="frequency",
xlab=expression(paste("volume (",mu, m^3,")", sep="")))
```

---

fitFun   *Model for the distribution of cell volumes*

Description

This is an implementation of a model for the distribution of cell volumes that constitutes Equation 7 in the paper listed in the references. It evaluates volEq7 at a vector of volume (μm^3) values.

Usage

```
fitFun(par,  t = 29, sigma_t = .3*t, V = 1:100)
```

Arguments

par	a list of parameter starting values, with elements A, r ($\mu m^3/h$), and sigma_r ($\mu m^3/h$)
t	a numeric value representing the average cell cycle time (h)
sigma_t	a numeric value representing the variability in the average cell cycle time t (h)
V	a numeric value representing the (vector of) volumes (μm^3) at which the model is to be evaluated

Value

A numeric vector representing a cell volume (μm^3) distribution.

References

Halter M, Elliott JT, Hubbard JB, Tona A, Plant AL (2009), "Cell Volume Distributions Reveal Cell Growth Rates and Division Times", Journal of Theoretical Biology, Vol 257, pp 124 - 130, DOI: 10.1016/j.jtbi.2008.10.031.

See Also

fitVolDist,fitFun

---

fitVolDist	*Fit a model for cell volume distribution under least squares criteria.*

Description

This function fits a model for cell volume distribution under least squares criteria; free model parameters are the cell growth rate r ($\mu m^3/h$), the variability in cell growth rate sigma_r ($\mu m^3/h$) and a linear scaling factor A.

Usage

```
fitVolDist(vol, freq, r = 100, sigma_r = 44, t = 40,
           sigma_t = 0.3 * t, maxiter = 100, nprint = 1,
           alg="leastsq")
```

Arguments

vol	a vector of numeric values representing volumes (μm^3)
freq	a vector of numeric values with the same length as vol, representing the frequency of cells of the volumes given in vol
r	a numeric value that represents the starting value for the rate ($\mu m^3/h$) of cell growth parameter
sigma_r	a numeric value that represents the starting value for the variability in the rate of cell growth parameter r ($\mu m^3/h$)

t	a numeric value representing the average cell cycle time (h)
sigma_t	a numeric value representing the variability in the average cell cycle time t (h)
maxiter	numeric value representing the maximum number of iterations used by nls.lm in model fitting under least squares criteria
nprint	optimization output is printed every nprint iterations
alg	character string indicating the algorithm to use; the choices are now "leastsq", so that that sum square error sum((data - model)^2) is minimized, or "chisq", so that the multinomial likelihood chi-square
	2*sum(data*log(data/model)) is minimized.

Value

fitVolDist returns an object of class "fitVolDist".

The generic accessor functions coefficients, vcov, deviance, fitted and residuals extract various useful features of the value returned by fitVolDist.

An object of class "fitVolDist" is a list containing the following components:

t	the value for t (h) used
sigma_t	the value for sigma_t (h) used
fitted	the model fit.
fit.res	the output object returned from nls.lm.
summary.fit.res	
	the summary of the output object returned from nls.lm.

References

Halter M, Elliott JT, Hubbard JB, Tona A, Plant AL (2009), "Cell Volume Distributions Reveal Cell Growth Rates and Division Times", Journal of Theoretical Biology, Vol 257, pp 124 - 130, DOI: 10.1016/j.jtbi.2008.10.031.

See Also

volEq7

Examples

```
## Not run:

##############################################################
# Fit volume distribution data for A10 vSMC cell cultures
# as described in the above referenced paper
##############################################################

## load the volume distributions in the "A10_vSMC_volume_data" dataset
data("A10_vSMC_volume_data")
labs <- c("a","b","c","d")
```

```
## the volume distributions representing 0 nM aphidicolin concentration
Aph0 <- list(Aph0_a, Aph0_b, Aph0_c, Aph0_d)
## the associated cell cycle times
tAph0 <- c(tAph0_a, tAph0_b, tAph0_c, tAph0_d)
## fit each dataset
Aph0res <- list()
Aph0tab <- matrix(ncol=2,nrow=4)
for(i in 1:length(Aph0)) {
  Aph0res[[i]] <- fitVolDist(vol=volumes_A10_vSMC, freq=Aph0[[i]],
                             r=100,sigma_r=44, t=tAph0[i])

  Aph0tab[i,] <- coef(Aph0res[[i]])
}
Aph0tab <- rbind(Aph0tab, colMeans(Aph0tab))
colnames(Aph0tab) <- c("r", "sigma_r")
rownames(Aph0tab) <- c(labs, "mean values")

## plot results
par(mfrow=c(3,2))

for(i in 1:length(Aph0)) {
  pe <- signif(coef(Aph0res[[i]]),3)
  plot(volumes_A10_vSMC, Aph0[[i]], type="l", main= substitute(paste(
  "r: ", p1, ", ", sigma[r],": ",p2),
  list(p1=pe[1], p2=pe[2])),
  xlab = expression(paste("volume (",mu, m^3,")", sep="")),
  sub=paste("vol. dist. Aphidicolin 0 nM", labs[i]), ylab="frequency")

  lines(volumes_A10_vSMC, fitted(Aph0res[[i]]), col=2)
}
textplot("(Above) Volume distribution data
representing A10 vSMC cells
cultured with 0 nM aphidicolin
concentration (black)
and model fit (red).
(Right) Parameter estimates and
mean estimates over the four fits",fixed.width=FALSE)
textplot(signif(Aph0tab,3))

## the volume distributions representing 50 nM aphidicolin concentration
Aph50 <- list(Aph50_a, Aph50_b, Aph50_c, Aph50_d)
## the associated cell cycle times
tAph50 <- c(tAph50_a, tAph50_b, tAph50_c, tAph50_d)
## fit each dataset
Aph50res <- list()
Aph50tab <- matrix(ncol=2,nrow=4)
for(i in 1:length(Aph50)) {
  Aph50res[[i]] <- fitVolDist(vol=volumes_A10_vSMC, freq=Aph50[[i]],
                              r=100,sigma_r=44, t=tAph50[i])

  Aph50tab[i,] <- coef(Aph50res[[i]])
}
```

```
Aph50tab <- rbind(Aph50tab, colMeans(Aph50tab))
colnames(Aph50tab) <- c("r", "sigma_r")
rownames(Aph50tab) <- c(labs, "mean values")

## plot results
par(mfrow=c(3,2))

for(i in 1:length(Aph50)) {
  pe <- signif(coef(Aph50res[[i]]),3)
  plot(volumes_A10_vSMC, Aph50[[i]], type="l", main= substitute(paste(
  "r: ", p1, ", ", sigma[r],": ",p2),
  list(p1=pe[1], p2=pe[2])),
  xlab = expression(paste("volume (", mu, m^3,")", sep="")),
  sub=paste("vol. dist. Aphidicolin 50 nM", labs[i]), ylab="frequency")

  lines(volumes_A10_vSMC, fitted(Aph50res[[i]]), col=2)
}
textplot("(Above) Volume distribution data
representing A10 vSMC cells
cultured with 50 nM aphidicolin
concentration (black)
and model fit (red).
(Right) Parameter estimates and
mean estimates over the four fits",fixed.width=FALSE)
textplot(signif(Aph50tab,3))

## the volume distributions representing 100 nM aphidicolin concentration
Aph100 <- list(Aph100_a, Aph100_b, Aph100_c, Aph100_d)
## the associated cell cycle times
tAph100 <- c(tAph100_a, tAph100_b, tAph100_c, tAph100_d)
## fit each dataset
Aph100res <- list()
Aph100tab <- matrix(ncol=2,nrow=4)
for(i in 1:length(Aph100)) {
  Aph100res[[i]] <- fitVolDist(vol=volumes_A10_vSMC, freq=Aph100[[i]],
                        r=100,sigma_r=44, t=tAph100[i])
  Aph100tab[i,] <- coef(Aph100res[[i]])
}
Aph100tab <- rbind(Aph100tab, colMeans(Aph100tab))
colnames(Aph100tab) <- c("r", "sigma_r")
rownames(Aph100tab) <- c(labs, "mean values")

## plot results
par(mfrow=c(3,2))

for(i in 1:length(Aph100)) {
  pe <- signif(coef(Aph100res[[i]]),3)
  plot(volumes_A10_vSMC, Aph100[[i]], type="l", main= substitute(paste(
  "r: ", p1, ", ", sigma[r],": ",p2),
  list(p1=pe[1], p2=pe[2])),
  xlab = expression(paste("volume (",mu, m^3,")", sep="")),
  sub=paste("vol. dist. Aphidicolin 100 nM", labs[i]), ylab="frequency")
```

```
  lines(volumes_A10_vSMC, fitted(Aph100res[[i]]), col=2)
}
textplot("(Above) Volume distribution data
representing A10 vSMC cells
cultured with 100 nM aphidicolin
concentration (black)
and model fit (red).
(Right) Parameter estimates and
mean estimates over the four fits",fixed.width=FALSE)
textplot(signif(Aph100tab,3))


## End(Not run)

##############################################################
# Fit volume distribution data for NIH3T3 cell cultures
# as described in the above referenced paper
##############################################################

## load the volume distributions in the "NIH3T3_volume_data" dataset
data("NIH3T3_volume_data")
labs <- c("a","b","c","d")

## the volume distributions representing NIH3T3 cells
NIH3T3 <- list(NIH3T3_a, NIH3T3_b, NIH3T3_c, NIH3T3_d)
## the associated cell cycle times
tNIH3T3 <- c(tNIH3T3_a, tNIH3T3_b, tNIH3T3_c, tNIH3T3_d)
## fit each dataset
NIH3T3res <- list()
NIH3T3tab <- matrix(ncol=2,nrow=4)
for(i in 1:length(NIH3T3)) {
  NIH3T3res[[i]] <- fitVolDist(vol=volumes_nih3t3, freq=NIH3T3[[i]],
                               r=100,sigma_r=44, t=tNIH3T3[i])
  NIH3T3tab[i,] <- coef(NIH3T3res[[i]])
}
NIH3T3tab <- rbind(NIH3T3tab, colMeans(NIH3T3tab))
colnames(NIH3T3tab) <- c("r", "sigma_r")
rownames(NIH3T3tab) <- c(labs, "mean values")

## plot results
par(mfrow=c(3,2))

for(i in 1:length(NIH3T3)) {
  pe <- signif(coef(NIH3T3res[[i]]),3)
  plot(volumes_nih3t3, NIH3T3[[i]], type="l", main= substitute(paste(
  "r: ", p1, ", ", sigma[r],": ",p2),
  list(p1=pe[1], p2=pe[2])),
  xlab = expression(paste("volume (",mu, m^3,")", sep="")),
  sub=paste("vol. dist. NIH3T3", labs[i]), ylab="frequency")

  lines(volumes_nih3t3, fitted(NIH3T3res[[i]]), col=2)
}
textplot("(Above) Volume distribution data
```

```
representing NIH3T3 cells
cultured under normal
conditions (black)
and model fit (red).
(Right) Parameter estimates and
mean estimates over the four fits",fixed.width=FALSE)
textplot(signif(NIH3T3tab,3))
```

NIH3T3_volume_data   *Volume distribution data for NIH3T3 cell cultures*

Description

Volume distribution data for NIH3T3 cell cultures under standard culture conditions

Usage

```
data(NIH3T3_volume_data)
```

Format

The data is formated as 4 numeric vectors of length 257 representing cell volume (μm^3) distributions, namely "NIH3T3_a", "NIH3T3_b", "NIH3T3_c", and "NIH3T3_d".

The estimated cell cycle time (h) for each volume distribution dataset is indicated in the numeric objects "tNIH3T3_a", "tNIH3T3_b", "tNIH3T3_c", and "tNIH3T3_d".

The object "volumes_nih3t3" is a numeric vector representing the volumes (μm^3) associated with all of the distributions.

Source

The measurement protocol is described in the paper in the references.

References

Halter M, Elliott JT, Hubbard JB, Tona A, Plant AL (2009), "Cell Volume Distributions Reveal Cell Growth Rates and Division Times", Journal of Theoretical Biology, Vol 257, pp 124 - 130, DOI: 10.1016/j.jtbi.2008.10.031.

Examples

```
data(NIH3T3_volume_data)
plot(volumes_nih3t3, NIH3T3_d,
main=expression(paste("Distribution of cell volumes (",mu,m^3,")", sep="")),
type="b", pch=20, ylab="frequency",
xlab=expression(paste("volume (",mu,m^3,")", sep="")))
```

---

volEq7   *Model for the distribution of cell volumes*

Description

This is an implementation of a model for the distribution of cell volumes (um^3) that constitutes Equation 7 in the paper listed in the references.

Usage

```
volEq7(A = 1, r = 1, sigma_r = 1,  t = 29, sigma_t = .3*t, V = 1)
```

Arguments

A	a numeric value that represents the starting value for a linear scaling parameter associated with the volume distribution curve
r	a numeric value that represents the starting value for the rate of cell growth parameter (h)
sigma_r	a numeric value that represents the starting value for the variability in the rate of cell growth parameter r (um^3/h)
t	a numeric value representing the average cell cycle time (h)
sigma_t	a numeric value representing the variability in the average cell cycle time t (h)
V	a numeric value representing the volume (um^3) at which the model is to be evaluated

Value

A numeric value representing the frequency of cells expected having volume V (um^3).

References

Halter M, Elliott JT, Hubbard JB, Tona A, Plant AL (2009), "Cell Volume Distributions Reveal Cell Growth Rates and Division Times", Journal of Theoretical Biology, Vol 257, pp 124 - 130, DOI: 10.1016/j.jtbi.2008.10.031.

See Also

fitVolDist

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