

Package ‘EKMCMC’

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Type Package

Title MCMC Procedures for Estimating Enzyme Kinetics Constants

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Description Functions for estimating catalytic constant and Michaelis-Menten constant for enzyme kinetics model using Metropolis-Hasting algorithm within Gibbs sampler based on the Bayesian framework. Additionally, a function to create plot to identify the goodness-of-fit is included.

License GPL-3

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catalytic_est

Estimation of single catalytic constant

Description

The function estimates catalytic constant using input data set and enzyme, substrate concentration, and MM constant.

Usage

```
catalytic_est(method = T, time, species, enz, subs, MM, catal,
  nrepeat = 10000, jump = 1, burning = 0, catal_m = 1,
  catal_v = 1e+06)
```

Arguments

method	method selection: T=TQ model, F=SQ model(default = T)
time	observed time interval
species	observed trajectory of product
enz	enzyme concentration
subs	substrate concentration
MM	true value of MM constant
catal	initial value of catalytic constant
nrepeat	total number of iteration (default=10000)
jump	length of distance (default =1)
burning	length of burning period (default =0)
catal_m	prior mean of gamma prior (default =1)
catal_v	prior variance of gamma prior (default =1e+6)

Details

The function `catalytic_est` generates a set of Monte Carlo simulation samples from posterior distribution of catalytic constant of enzyme kinetics model. Because the function considers catalytic constant as a parameter to be estimated, the user should input three constants of enzyme concentration, substrate concentration and Michaelis-Menten constant.

Value

A vector of posterior samples of catalytic constant

Examples

```
data("Chymo_low")
time1=Chymo_low[,1]
species1=Chymo_low[,2]
Chymotrypsin.low<-catalytic_est(method=TRUE,time=time1,species=species1,enz=4.4e+7,subs=4.4e+7
,MM=4.4e+8, catal=0.1,nrepeat = 10000)
```

Chymo_high

Product concentration of 101 observed time

Description

An artificial data set containing the product concentration and it's observed time based on high enzyme concentration and low substrate concentration

Usage

Chymo_high

Format

A data frame with 101 rows and 2 variables:

time observed time, no unit

product product concentration, no unit

Chymo_low

Product concentration of 101 observed time

Description

An artificial data set containing the product concentration and it's observed time based on low enzyme concentration and low substrate concentration

Usage

Chymo_low

Format

A data frame with 101 rows and 2 variables:

time observed time, no unit

product product concentration, no unit

combined_est	<i>Simultaneous estimation of Michaelis-Menten constant and catalytic constant using combined data</i>
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Description

The function estimates both catalytic and MM constant simultaneously using combined data sets for different enzyme concentrations and substrate concentrations for two input data sets according to the different values of enzyme concentrations or substrate concentration.

Usage

```
combined_est(method = T, time1, time2, species1, species2, enz1, enz2, subs1,
  subs2, MM, catal, tun = 2.4, std, nrepeat, jump = 1, burning = 0,
  catal_m = 1, catal_v = 1e+05, MM_m = 1, MM_v = 1e+05)
```

Arguments

method	method selection: T=TQ model, F=SQ model(default = T)
time1	observed time interval for data1
time2	observed time interval for data2
species1	observed trajectory of product for data1
species2	observed trajectory of product for data2
enz1	enzyme concentration for data1
enz2	enzyme concentration for data2
subs1	substrate concentration for data1
subs2	substrate concentration for data2
MM	initial value of MM constant
catal	initial value of catalytic constant
tun	tunning constant of MH algorithm (default =2.4)
std	standard deviation of proposal distribution
nrepeat	total number of iteration
jump	length of distance (default =1)
burning	length of burning period (default =0)
catal_m	prior mean of gamma prior (default =1)
catal_v	prior variance of gamma prior (default =10000)
MM_m	prior mean of gamma prior (default =1)
MM_v	prior variance of gamma prior (default =10000)

Details

The function `combined_est` generates a set of Markov Chain Monte Carlo simulation samples from the posterior distribution of MM and catalytic constant of enzyme kinetics model. Because the function considers both MM constant and catalytic constant as parameters to be estimated, the user should input constants of enzyme concentrations, substrate concentrations. Because this function utilizes two data sets according to the different values of enzyme concentration or substrate concentration the user inputs two sets of information of input data set, enzyme concentration, and substrate concentration. prior information for both two parameter can be given. The turning constant and standard deviation can be set to controlled proper mixing and acceptance ratio of MM constant from it's conditional posterior distribution. Posterior samples are only stored with fixed interval according to set "jump" to reduce serial correlation The initial iterations are removed for convergence. The burning is set the length of initial iterations.

Value

A $n \times 2$ matrix of postrior samples of catalytic constant and MM constant

Examples

```
data("Chymo_low")
time1=Chymo_low[,1]
species1=Chymo_low[,2]
data("Chymo_high")
time2=Chymo_high[,1]
species2=Chymo_high[,2]
enz.Chymotrypsin<-combined_est(method=TRUE, time1=time1 ,time2=time2 ,species1=species1
, species2=species2,enz1=4.4e+7,enz2=4.4e+9
, subs1=4.4e+7,subs2=4.4e+7,MM=1e+9,catal=0.01,
tun=2.0,std=8e+7,nrepeat=1000,jump=10,burning=0
,catal_m=1,catal_v=1e+6, MM_m=1,MM_v=1e+10)
```

fore_p

Simulation plot of enzyme kinetics model

Description

The function depicts the overlaid two plots; one is observed data, the other is simulation result using fitted MM constant and catalytic constant.

Usage

```
fore_p(method = TRUE, CL = TRUE, time, species, enz, subs, MM, catal,
nrepeat = 100, ti = 1)
```

Arguments

method	method selection: T=TQ model, F=SQ model(default = T)
CL	Adding empirical 95% confidence interval (default = T)
time	observed time interval
species	observed trajectory of product
enz	enzyme concentration
subs	substrate concentration
MM	true value of MM constant
catal	initial value of catalytic constant
nrepeat	total number of simulation (default=100)
ti	time interval for discretized simulation result (default =1)

Details

Basically this function draws overlaid picture: The one is trajectory of given data of products for enzyme kinetics model. The other is trajectory of products from simulation result of Gillespie algorithm with estimated two constants, Michaelis-Menten constant and catalytic constant. CL option controls the plot that depicts the observed data and mean of simulated series only or adding 95 confidence interval with 10 samples of simulated trajectory.

Value

This function has no returned object.

Examples

```
data("Chymo_low")
time1=Chymo_low[,1]
species1=Chymo_low[,2]
fore_p(method=TRUE, CL=TRUE, time=time1, species=species1,enz=4.4e+7, subs=4.4e+7
,MM=4.4e+8, catal=.051)
```

MM_catal_est

Simultaneous estimation of Michaelis-Menten constant and catalytic constant

Description

The function estimates both catalytic and MM constant simultaneously with given enzyme concentration and substrate concentration.

Usage

```
MM_catal_est(method = T, time, species, enz, subs, MM, catal, tun = 2.4,
std, nrepeat, jump = 1, burning = 0, catal_m = 1, catal_v = 10000,
MM_m = 1, MM_v = 10000)
```

Arguments

method	method selection: T=TQ model, F=SQ model(default = T)
time	observed time interval
species	observed trajectory of product
enz	enzyme concentration
subs	substrate concentration
MM	true value of MM constant
catal	initial value of catalytic constant
tun	tunning constant of MH algorithm (default=2.4)
std	standard deviation of proposal distribution (if =0, caclulated by Opt. function)
nrepeat	total number of iteration (default=10000)
jump	length of distance (default =1)
burning	lenth of burning period (default =0)
catal_m	prior mean of gamma prior (default =1)
catal_v	prior variance of gamma prior (default =10000)
MM_m	prior mean of gamma prior (default =1)
MM_v	prior variance of gamma prior (default =10000)

Details

The function `MM_catal_est` generates a set of Markov Chain Monte Carlo simulation samples from the posterior distribution of MM and catalytic constant of enzyme kinetics model. Because the function considers both MM constant and catalytic constant as parameters to be estimated, the user should input constants of enzyme concentration, substrate concentration. prior information for both two parameter can be given. The turning constant and standard deviation can be set to controlled proper mixing and acceptance ratio of MM constant from it's conditional posterior distribution. Posterior samples are only stored with fixed interval according to set "jump" to reduce serial correlation. The initial iterations are removed for convergence. The burning is set the length of initial iterations.

Value

A $n \times 2$ matrix of posterior samples of catalytic constant and MM constant

Examples

```
data("Chymo_low")
time1=Chymo_low[,1]
species1=Chymo_low[,2]
Chymotrypsin.low<-MM_catal_est(method=TRUE, time=time1,species=species1,enz=4.4e+7
,subs=4.4e+7,MM=1e+9,catal=0.01,tun=2.4,std=8e+7,nrepeat=1000,jump=10,
burning=0,catal_m=1,catal_v=1e+10, MM_m=1e+9,MM_v=1e+18)
```

MM_est *Estimation of single Michaelis-Menten constant*

Description

The function estimates MM constant using input data set and enzyme, substrate concentration, and catalytic constant.

Usage

```
MM_est(method = T, time, species, enz, subs, MM, catal, tun = 2.4, std,
        nrepeat, jump = 1, burning = 0, MM_m = 1, MM_v = 1e+06)
```

Arguments

method	method selection: T=TQ model, F=SQ model(default = T)
time	observed time interval
species	observed trajectory of product
enz	enzyme concentration
subs	substrate concentration
MM	initial value of MM constant
catal	true value of catalytic constant
tun	tunning constant of MH algorithm (default=2.4)
std	standard deviation of proposal distribution (if =0, cacluated by Opt. function)
nrepeat	total number of iteration (default=10000)
jump	length of distance (default =1)
burning	lenth of burning period (default =0)
MM_m	prior mean of gamma prior (default =1)
MM_v	prior variance of gamma prior (default =10000)

Details

The function MM_est generates a set of Markov Chain Monte Carlo simulation samples from posterior distribution of MM constant of enzyme kinetics model. Because the function considers MM constant as a parameter to be estimated, the user should input three constants of enzyme concentration, substrate concentration and catalytic constant. prior information for MM constant can be given. The turning constant and standard deviation can be set to controlled proper mixing and acceptance ratio of MM constant from it's posterior distribution. Posterior samples are only stored with fixed interval according to set "jump" to reduce serial correlation The initial iterations are removed for convergence. The burning is set the length of initial iterations.

Value

A vector of posterior samples of Michaelis-Menten constant

Examples

```
data("Chymo_low")
time1=Chymo_low[,1]
species1=Chymo_low[,2]
Chymotrypsin.mm<-MM_est(method=TRUE,time=time1,species=species1,enz=4.4e+7,subs=4.4e+7
,MM=10000,catal=0.051,tun=2.4,std=8e+7 ,nrepeat=1000,jump=10
,burning=0,MM_m=1,MM_v=1e+10)
```

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