Package ‘SIfEK’

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Type Package

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Description
Functions for estimating catalytic constant and Michaelis-Menten constant (MM constant) of stochastic Michaelis-Menten enzyme kinetics model are provided. The likelihood functions based on stochastic simulation approximation (SSA), diffusion approximation (DA), and Gaussian processes (GP) are provided to construct posterior functions for the Bayesian estimation. All functions utilize Markov Chain Monte Carlo (MCMC) methods with Metropolis-Hastings algorithm with random walk chain and robust adaptive Metropolis-Hastings algorithm based on Bayesian framework.

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R topics documented:

`Chymo_high` *Product concentration of 101 observed time*

Description

A synthetic data set of the product concentration of the enzyme kinetics with lower initial enzyme concentration and discrete observed time.

Usage

```
Chymo_high
```

Format

A data frame with 101 rows and 2 variables

`Chymo_low` *Product concentration of 101 observed time*

Description

A synthetic data set of the product concentration of the enzyme kinetics with higher initial enzyme concentration and discrete observed time.

Usage

```
Chymo_low
```

Format

A data frame with 101 rows and 2 variables

DA.cat — *Estimation of single catalytic constant using the diffusion approximation*

Description

The function estimates single catalytic constant using single data set with an initial enzyme concentrations and substrate concentration. The diffusion approximation is utilized for the likelihood function.

Usage

```
DA.cat(method = T, dat, enz, subs, MM, catal, nrepeat = 10000,
  jump = 1, burning = 0, catal_m_v = c(1, 10000), sig,
  scale_tun = 80)
```

Arguments

`method`	method selection: T=TQ model, F=SQ model(default = T)
`dat`	observed dataset (time & trajectory columns)
`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`	lenth of burning period (default =0)
`catal_m_v`	Catalytic prior gamma mean, variance(default=c(1,10000))
`sig`	standard deviation of univariate Normal proposal distribution
`scale_tun`	scale tunning constant for stochastic simulation

Details

The function DA.cat generates a set of MCMC simulation samples from the conditional posterior distribution of catalytic constant of enzyme kinetics model. As the catalytic constant is only parameter to be estimated in the function the user should assign MM constant as well as initial enzyme concentration and substrate concentration. The prior information for the parameter can be given. The turning constant (scale_tun) and standard deviation (sig) can be set to controlled proper mixing and acceptance ratio of the parameter from the conditional posterior distribution. The 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. The diffusion approximation method is used for construction of the likelihood.

Value

A vector of posterior samples of catalytic constant

Examples

```
## Not run:
data('Chymo_low')
sk_DA=DA.cat(method=TRUE,dat=Chymo_low,enz=4.4e+7,subs = 4.4e+7,MM=4.4e+8,catal=0.05
                ,nrepeat=10000,jump=1,burning = 0,catal_m_v=c(1,10000),sig=0.005)

## End(Not run)
```

DA.combi *Simultaneous estimation of Michaelis-Menten constant and catalytic constant using combined data and the likelihood function with the diffusion approximation method.*

Description

The function estimates both catalytic constant and Michaelis-Menten constant simultaneously using combined data sets with different enzyme concentrations or substrate concentrations. The diffusion approximation is utilized for the likelihood function.

Usage

```
DA.combi(method = T, dat1, dat2, enz, subs, MM, catal, sig,
  nrepeat = 11000, jump = 1, burning = 1000, catal_m_v = c(1,
  10000), MM_m_v = c(1, 10000), scale_tun = 80)
```

Arguments

`method`	method selection: T=TQ model, F=SQ model(default = T)
`dat1`	observed dataset1 (time & trajectory columns)
`dat2`	observed dataset2 (time & trajectory columns)
`enz`	enzyme concentrate
`subs`	substrate concentrate
`MM`	initial value of MM constant
`catal`	initial value of catalytic constant
`sig`	variance of bivariate Normal proposal distribution
`nrepeat`	total number of iteration (default=10000)
`jump`	length of distance (default =1)
`burning`	length of burning period (default =0)
`catal_m_v`	catalytic prior gamma mean, variance(default=c(1,10000))
`MM_m_v`	MM prior gamma mean, variance(default=c(1,10000))
`scale_tun`	scale tunning constant for stochastic simulation

Details

The function DA.combi generates a set of MCMC simulation samples from the posterior distribution of catalytic constant and MM constant of enzyme kinetics model. As the function uses combined data set with different initial concentration of enzyme or substrate concentration the user should input two values of enzyme and substrate initial concentration. The prior information for both two parameters can be given. The turning constant (scale_tun) and variances for two constants (sig) can be set to controlled proper mixing and acceptance ratio for updating two parameters simultaneously. The 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. The diffusion approximation method is used for construction of the likelihood.

Value

A n*2 matrix of postrior samples of catalytic constant and MM constant

Examples

```
## Not run:
data('Chymo_low')
data('Chymo_high')
comb_DA=DA.combi(method=TRUE,dat1=Chymo_low,dat2=Chymo_high,enz=c(4.4e+7,4.4e+9)
               ,subs=c(4.4e+7,4.4e+7),MM=4.4e+8,catal=0.05,sig=2.0*(c(0.005,8e+7))^2
               ,nrepeat=10000,jump=1,burning=0,catal_m_v = c(1, 1e+6)
               ,MM_m_v = c(1, 1e+10),scale_tun=100)

## End(Not run)
```

DA.MM *Estimation of single Michaelis-Menten constant using diffusion approximation*

Description

The function estimates single Michaelis-Menten constant using the likelihood function with diffusion approximation method.

Usage

```
DA.MM(method = T, dat, enz, subs, MM, catal, nrepeat = 10000,
  jump = 1, burning = 0, MM_m_v = c(1, 10000), sig, scale_tun = 80)
```

Arguments

method	method selection: T=TQ model, F=SQ model(default = T)
dat	observed dataset (time & trajectory columns)
enz	enzyme concentrate
subs	substrate concentrate
MM	initial value of MM constant
catal	true value of catalytic constant
nrepeat	total number of iteration (default=10000)
jump	length of distance (default = 1)
burning	length of burning period (default=0)
MM_m_v	MM prior gamma mean, variance(default=c(1,10000))
sig	standard deviation of univariate Normal proposal distribution
scale_tun	scale tunning constant for stochastic simulation

Details

The function DA.MM generates a set of MCMC simulation samples from the conditional posterior distribution of Michaelis-Menten constant of enzyme kinetics model. As the MM constant is only parameter to be estimated in the function the user should assign catalytic constant as well as initial enzyme concentration and substrate concentration. The prior information for the parameter can be given. The turning constant (scale_tun) and standard deviation (sig) can be set to controlled proper mixing and acceptance ratio of the parameter from the conditional posterior distribution. The 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. The diffusion approximation method is used for construction of the likelihood.

Value

A vector of posterior samples of catalytic constant

Examples

```
## Not run:
data('Chymo_low')
sm_DA=DA.MM(method=TRUE,dat=Chymo_low,enz=4.4e+7,subs = 4.4e+7,MM=4.4e+8,catal=0.05
                 ,nrepeat=10000,jump=1,burning = 0,MM_m_v=c(1,1e+10),sig=500)

## End(Not run)
```

DA.multi *Simultaneous estimation of Michaelis-Menten constant and catalytic constant using the likelihood function with diffusion approximation method*

Description

The function estimates both catalytic constant and Michaelis-Menten constant simultaneously using single data set with an initial enzyme concentrations and substrate concentration. The diffusion approximation is utilized for the likelihood function.

Usage

```
DA.multi(method = T, dat, enz, subs, MM, catal, nrepeat = 10000,
  jump = 1, burning, catal_m_v = c(1, 10000), MM_m_v = c(1, 10000),
  sig, scale_tun = 80)
```

Arguments

`method`	method selection: T=TQ model, F=SQ model(default = T)
`dat`	observed dataset (time & trajectory columns)
`enz`	enzyme concentrate
`subs`	substrate concentrate
`MM`	initial 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_v`	catalytic prior gamma mean, variance(default=c(1,10000))
`MM_m_v`	MM prior gamma mean, variance(default=c(1,10000))
`sig`	variance of bivariate Normal proposal distribution
`scale_tun`	scale tunning constant for stochastic simulation

Details

The function DA.multi generates a set of MCMC simulation samples from the posterior distribution of catalytic constant and MM constant of enzyme kinetics model. As the function estimates both two constants the user should input the enzyme and substrate initial concentration. The prior information for both two parameters can be given. The turning constant (scale_tun) and variances for two constants (sig) can be set to controlled proper mixing and acceptance ratio for updating two parameters simultaneously. The 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. The diffusion approximation method is used for construction of the likelihood.

Value

A n*2 matrix of postrior samples of catalytic constant and MM constant

Examples

```
## Not run:
data('Chymo_low')
dou_DA=DA.multi(method=TRUE,dat=Chymo_low,enz=4.4e+7,subs=4.4e+7,MM=4.4e+8,catal=0.05
               ,nrepeat=10000,jump=1,burning=1,catal_m_v=c(1,1e+10),MM_m_v=c(1e+9,1e+18)
                ,sig=2.4*0.001*c(0.05,4.4e+8),scale_tun=80)

## End(Not run)
```

GP.cat *Estimation of single catalytic constant using Gaussian processes*

Description

The function estimates single catalytic constant using single data set with an initial enzyme concentrations and substrate concentration. The Gaussian processes is utilized for the likelihood function.

Usage

```
GP.cat(method = T, RAM = F, time, dat, enz, subs, MM, catal,
  nrepeat = 10000, jump = 1, burning = 0, catal_m_v = c(1, 10000),
  sig, va)
```

Arguments

method	method selection: T=TQ model, F=SQ model(default = T)
RAM	Robust Adaptive MCMC options (default = F)
time	total time of data
dat	observed dataset (trajectory column)
enz	enzyme concentrate
subs	substrate concentrate
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_v	Catalytic prior gamma mean, variance(default=c(1,10000))
sig	standard deviation of univariate Normal proposal distribution
va	variance of dataset

Details

The function GP.cat generates a set of MCMC simulation samples from the conditional posterior distribution of catalytic constant of enzyme kinetics model. As the catalytic constant is only parameter to be estimated in the function the user should assign MM constant as well as initial enzyme concentration and substrate concentration. The prior information for the parameter can be given. The GP.cat function can select Robust Adaptive Metropolis (RAM) algorithm as well as Metropolis-Hastings algorithm with random walk chain for MCMC procedure. When "RAM" is assigned T then the function use RAM method and the "sig" is used as initial standard deviation of normal proposal distribution. When "RAM" is F, the function use Metropolis-Hastings algorithm with random walk chain and the "sig" can be set to controlled proper mixing and acceptance ratio of the parameter from the conditional posterior distribution. The "va" is the variance of the Gaussian process. The 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. The Gaussian process method is used for construction of the likelihood.

Value

A vector of posterior samples of catalytic constant

Examples

```
## Not run:
data('Chymo_low')
time1=max(Chymo_low[,1])*1.01
sk_GPMH=GP.cat(method=TRUE,time=time1,dat=Chymo_low[,2],enz=4.4e+7,subs=4.4e+7
                      ,MM=4.4e+8,catal=0.05,nrepeat=10000,jump=1,burning=0
                      ,catal_m_v=c(1,10000),sig=0.016,va=var(Chymo_low[,2]))
# use RAM algorithm #
sk_GPRAM=GP.cat(method=TRUE,RAM=TRUE,time=time1,dat=Chymo_low[,2],enz=4.4e+7,subs=4.4e+7
                      ,MM=4.4e+8,catal=0.05,nrepeat=10000,jump=1,burning=0
                      ,catal_m_v=c(1,10000),sig=0.1,va=var(Chymo_low[,2]))

## End(Not run)
```

`GP.combi` *Simultaneous estimation of Michaelis-Menten constant and catalytic constant using combined data and the likelihood function with the Gaussian process method*

Description

The function estimates both catalytic constant and Michaelis-Menten constant simultaneously using combined data sets with different enzyme concentrations or substrate concentrations. The Gaussian process is utilized for the likelihood function.

Usage

```
GP.combi(method = T, RAM = F, time1, dat1, time2, dat2, enz, subs, MM,
  catal, nrepeat = 11000, jump = 1, burning = 1000,
  catal_m_v = c(1, 10000), MM_m_v = c(1, 10000), sig, va)
```

Arguments

`method`	method selection: T=TQ model, F=SQ model(default = T)
`RAM`	Robust Adaptive MCMC options (default = F)
`time1`	total time of dataset1
`dat1`	observed dataset1 (trajectory column)
`time2`	total time of dataset2
`dat2`	observed dataset2 (trajectory column)
`enz`	enzyme concentrate
`subs`	substrate concentrate
`MM`	initial value of MM constant
`catal`	initial value of catalytic constant
`nrepeat`	total number of iteration (defuault=10000)
`jump`	length of distance (default =1)
`burning`	length of burning period (default =0)
`catal_m_v`	catalytic prior gamma mean, variance(default=c(1,10000))
`MM_m_v`	MM prior gamma mean, variance(default=c(1,10000))
`sig`	variance of bivariate Normal proposal distribution
`va`	variance of data

Details

The function GP.combi generates a set of MCMC simulation samples from the posterior distribution of catalytic constant and MM constant of enzyme kinetics model. As the function uses combined data set with different initial concentration of enzyme or substrate concentration the user should input two values of enzyme and substrate initial concentration. The prior information for both two parameters can be given. The function can select Robust Adaptive Metropolis (RAM) algorithm as well as Metropolis-Hastings algorithm with random walk chain for MCMC procedure. When “RAM” is assigned T then the function use RAM method and the “sig” is used as initial variances of normal proposal distribution for catalytic and MM constant. When “RAM” is F, the function use Metropolis-Hastings algorithm with random walk chain and the “sig” can be set to controlled proper mixing and acceptance ratio of the parameter for updating two parameters simultaneously. The “va” is the variance of the Gaussian process. The 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. The Gaussian process method is used for construction of the likelihood

Value

A n*2 matrix of postrior samples of catalytic constant and MM constant

Examples

```
## Not run:
data('Chymo_low')
data('Chymo_high')
time1 = max(Chymo_low[,1])*1.01
time2 = max(Chymo_high[,1])*1.01
comb_GPMH=GP.combi(method=TRUE,dat1=Chymo_low[,2],time1=time1,dat2=Chymo_high[,2],time2=time2
                  ,enz=c(4.4e+7,4.4e+9),subs=4.4e+7,MM=4.4e+8,catal=0.05,nrepeat=10000
                  ,jump=1,burning=0,catal_m_v=c(1,1e+10),MM_m_v=c(1e+9,1e+18)
                  ,sig=c(0.005,4.4e+8)^2,va=c(var(Chymo_low[,2]),var(Chymo_high[,2])))

# use RAM algorithm #
comb_GPRAM=GP.combi(method=TRUE,RAM=TRUE,dat1=Chymo_low[,2],time1=time1,dat2=Chymo_high[,2]
                      ,time2=time2,enz=c(4.4e+7,4.4e+9),subs=4.4e+7,MM=4.4e+8,catal=0.05
                  ,nrepeat=10000,jump=1,burning=0,catal_m_v=c(1, 1e+6),MM_m_v=c(1,1e+10)
                     ,sig=c(1,1e+11),va=c(var(Chymo_low[,2]),var(Chymo_high[,2])))

## End(Not run)
```

GP.MM

Estimation of single Michaelis-Menten constant using the Gaussian process method The function estimates single Michaelis-Menten constant using the likelihood function with the Gaussian process method.

Description

Estimation of single Michaelis-Menten constant using the Gaussian process method The function estimates single Michaelis-Menten constant using the likelihood function with the Gaussian process method.

Usage

```
GP.MM(method = T, RAM = F, time, dat, enz, subs, MM, catal,
  nrepeat = 10000, jump = 1, burning = 0, MM_m_v = c(1, 10000),
  sig, va)
```

Arguments

`method`	method selection: T=TQ model, F=SQ model(default = T)
`RAM`	Robust Adaptive MCMC options (default = F)
`time`	total time of data
`dat`	observed dataset (trajectory column)
`enz`	enzyme concentrate
`subs`	substrate concentrate
`MM`	initial value of MM constant

catal	true value of catalytic constant
nrepeat	total number of iteration (default=10000)
jump	length of distance (default = 1)
burning	length of burning period (default=0)
MM_m_v	MM prior gamma mean, variance(default=c(1,10000))
sig	standard deviation of univariate Normal proposal distribution
va	variance of dataset

Details

The function GP.MM generates a set of MCMC simulation samples from the conditional posterior distribution of Michaelis-Menten constant of enzyme kinetics model. As the MM constant is only parameter to be estimated in the function the user should assign catalytic constant as well as initial enzyme concentration and substrate concentration. The prior information for the parameter can be given. The GP.MM function can select Robust Adaptive Metropolis (RAM) algorithm as well as Metropolis-Hastings algorithm with random walk chain for MCMC procedure. When “RAM” is assigned T then the function use RAM method and the “sig” is used as initial standard deviation of normal proposal distribution. When “RAM” is F, the function use Metropolis-Hastings algorithm with random walk chain and the “sig” can be set to controlled proper mixing and acceptance ratio of the parameter from the conditional posterior distribution. The “va” is the variance of the Gaussian process. The 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. The diffusion approximation method is used for construction of the likelihood.

Value

A vector of posterior samples of catalytic constant

Examples

```
## Not run:
data('Chymo_low')
time1=max(Chymo_low[,1])*1.01
sm_GPMH=GP.MM(method=TRUE,time=time1,dat=Chymo_low[,2],enz=4.4e+7,subs=4.4e+7
                      ,MM=4.4e+8,catal=0.05,nrepeat=10000,jump=1,burning=0
                      ,MM_m_v=c(1,1e+10),sig=8e+7,va=var(Chymo_low[,2]))
# use RAM algorithm #
sm_GPRAM=GP.MM(method=TRUE,RAM=TRUE,time=time1,dat=Chymo_low[,2],enz=4.4e+7,subs=4.4e+7
                        ,MM=4.4e+8,catal=0.05,nrepeat=10000,jump=1,burning=0
                        ,MM_m_v=c(1,1e+10),sig=500,va=var(Chymo_low[,2]))

## End(Not run)
```

GP.multi — *Simultaneous estimation of Michaelis-Menten constant and catalytic constant using the likelihood function with the Gaussian process method.*

Description

The function estimates both catalytic constant and Michaelis-Menten constant simultaneously using single data set with an initial enzyme concentrations and substrate concentration. the Gaussian process is utilized for the likelihood function.

Usage

```
GP.multi(method = T, RAM = F, time, dat, enz, subs, MM, catal,
  nrepeat = 10000, jump = 1, burning = 0, catal_m_v = c(1, 10000),
  MM_m_v = c(1, 10000), sig, va)
```

Arguments

`method`	method selection: T=TQ model, F=SQ model(default = T)
`RAM`	Robust Adaptive MCMC options (default = F)
`time`	total time of data
`dat`	observed dataset (trajectory column)
`enz`	enzyme concentrate
`subs`	substrate concentrate
`MM`	initial value of MM constant
`catal`	initial value of cataldattic constant
`nrepeat`	total number of iteration (default=10000)
`jump`	length of distance (default =1)
`burning`	length of burning period (default =0)
`catal_m_v`	MM prior gamma mean, variance(default=c(1,10000))
`MM_m_v`	MM prior gamma mean, variance(default=c(1,10000))
`sig`	variance of bivariate Normal proposal distribution
`va`	variance of dataset

Details

The function GP.multi generates a set of MCMC simulation samples from the posterior distribution of catalytic constant and MM constant of enzyme kinetics model. As the function estimates both two constants the user should input the enzyme and substrate initial concentration. The prior information for both two parameters can be given. The function can select Robust Adaptive Metropolis (RAM) algorithm as well as Metropolis-Hastings algorithm with random walk chain for MCMC procedure. When “RAM” is assigned T then the function use RAM method and the “sig” is used as initial variances of normal proposal distribution for catalytic and MM constant. When “RAM” is F, the function use Metropolis-Hastings algorithm with random walk chain and the “sig” can be set to controlled proper mixing and acceptance ratio of the parameter for updating two parameters simultaneously. The “va” is the variance of the Gaussian process. The 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. The diffusion approximation method is used for construction of the likelihood

Value

A vector of posterior samples of catalytic constant

Examples

```
## Not run:
data('Chymo_low')
time1=max(Chymo_low[,1])*1.01
dou_GPMH=GP.multi(method=TRUE,time=time1,dat=Chymo_low[,2],enz=4.4e+7,subs=4.4e+7
                ,MM=4.4e+8,catal=0.05,nrepeat=10000,jump=1,burning=0,catal_m_v=c(1,1e+10)
                    ,MM_m_v=c(1e+9,1e+18),sig=c(0.05,4.4e+8)^2,va=var(Chymo_low[,2]))
# use RAM algorithm #
dou_GPRAM=GP.multi(method=TRUE,RAM=TRUE,time=time1,dat=Chymo_low[,2],enz=4.4e+7,subs=4.4e+7
                  ,MM=4.4e+8,catal=0.05,nrepeat=10000,jump=1,burning=0,catal_m_v=c(1,1e+10)
                      ,MM_m_v=c(1e+9,1e+18),sig=c(1,1),va=var(Chymo_low[,2]))

## End(Not run)
```

SSA.cat *Estimation of single catalytic constant using the stochastic simulation approximation method*

Description

The function estimates single catalytic constant using single data set with an initial enzyme concentrations and substrate concentration. The stochastic simulation approximation method is utilized for the likelihood function.

Usage

```
SSA.cat(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`	lenth 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 SSA.cat generates a set of Monte Carlo simulation samples from the conditional posterior distribution of catalytic constant of enzyme kinetics model. As the catalytic constant is only parameter to be estimated in the function the user should assign MM constant as well as initial enzyme concentration and substrate concentration. The prior information for the parameter can be given.

Value

A vector of posterior samples of catalytic constant

Examples

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

`SSA.combi` *Simultaneous estimation of Michaelis-Menten constant and catalytic constant using combined data and the likelihood function with the Stochastic Simulation Approximation method.*

Description

The function estimates both catalytic constant and Michaelis-Menten constant simultaneously using combined data sets with different enzyme concentrations or substrate concentrations. The diffusion approximation is utilized for the likelihood function.

Usage

```
SSA.combi(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`	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 DA.combi generates a set of MCMC simulation samples from the posterior distribution of catalytic constant and MM constant of enzyme kinetics model. As the function uses combined data set with different initial concentration of enzyme or substrate concentration the user should input two values of enzyme and substrate initial concentration. The prior information for both two parameters can be given. The function utilizes the Gibbs sampler to update two parameters iteratively from conditional posterior distribution. Updating catalytic constant is conducted using conditional gamma distribution. The posterior samples of MM constant are drawn vis Metropolis-Hasting algorithm with random walk chain. The turning constant (scale_tun) and standard deviation of proposal normal distribution (sig) can be set to controlled proper mixing and acceptance ratio of the parameter from the conditional posterior distribution. The 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. The stochastic simulation approximation method is used for construction of the likelihood.

Value

A n*2 matrix of postrior samples of catalytic constant and MM constant

Examples

```
## Not run:
data("Chymo_low")
time1=Chymo_low[,1]
species1=Chymo_low[,2]
data("Chymo_high")
time2=Chymo_high[,1]
species2=Chymo_high[,2]
enz.Chymotrypsin<-SSA.combi(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=10000,jump=1,burning=0
                               ,catal_m=1,catal_v=1e+6, MM_m=1,MM_v=1e+10)

## End(Not run)
```

SSA.MM — *Estimation of single Michaelis-Menten constant using the stochastic simulation approximation*

Description

The function estimates single Michaelis-Menten constant using the likelihood function with the stochastic simulation approximation method.

Usage

```
SSA.MM(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, caclulated 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 SSA.MM generates a set of MCMC simulation samples from the conditional posterior distribution of Michaelis-Menten constant of enzyme kinetics model. As the MM constant is only parameter to be estimated in the function the user should assign catalytic constant as well as initial enzyme concentration and substrate concentration. The prior information for the parameter can be given. The turning constant (scale_tun) and standard deviation of proposal normal distribution (sig) can be set to controlled proper mixing and acceptance ratio of the parameter from the conditional posterior distribution. The 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. The diffusion approximation method is used for construction of the likelihood.

Value

A vector of posterior samples of Michaelis-Menten constant

Examples

```
data("Chymo_low")
time1=Chymo_low[,1]
species1=Chymo_low[,2]
 Chymotrypsin.mm<-SSA.MM(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=10000,jump=1
 ,burning=0,MM_m=1,MM_v=1e+10)
```

SSA.multi

Simultaneous estimation of Michaelis-Menten constant and catalytic constant using the likelihood function with the stochastic simulation approximation method

Description

The function estimates both catalytic constant and Michaelis-Menten constant simultaneously using single data set with an initial enzyme concentrations and substrate concentration. The stochastic simulation approximation is utilized for the likelihood function

Usage

```
SSA.multi(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 DA.multi generates a set of MCMC simulation samples from the posterior distribution of catalytic constant and MM constant of enzyme kinetics model. As the function estimates both two constants the user should input the enzyme and substrate initial concentration. The prior information for both two parameters can be given. The function utilizes the Gibbs sampler to update two parameters iteratively from conditional posterior distribution. Updating catalytic constant is conducted using conditional gamma distribution. The posterior samples of MM constant are drawn vis Metropolis-Hasting algorithm with random walk chain. The turning constant (scale_tun) and standard deviation of proposal normal distribution (sig) can be set to controlled proper mixing and acceptance ratio of the parameter from the conditional posterior distribution. The 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. The stochastic simulation approximation method is used for construction of the likelihood.

Value

A n*2 matrix of postrior samples of catalytic constant and MM constant

Examples

```
data(”Chymo_low”)
time1=Chymo_low[,1]
species1=Chymo_low[,2]
Chymotrypsin.low<-SSA.multi(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=10000,jump=1,
burning=0,catal_m=1,catal_v=1e+10, MM_m=1e+9,MM_v=1e+18)
```

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