

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.

License GPL-3

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catalytic_est *Function for estimating the catalytic constant*

Description

The function estimates catalytic constant using progress-curve data, enzyme concentrations, substrate concentrations, and the Michaelis-Meten constant.

Usage

```
catalytic_est(
  method,
  timespan,
  products,
  enz,
  subs,
  K_M,
  catal_m,
  catal_v,
  nrepeat,
  jump,
  burn,
  volume,
  t_unit,
  c_unit
)
```

Arguments

| | |
|----------|--|
| method | This determines which model, the sQSSA or tQSSA model, is used for the estimation. Specifically, the input for method is TRUE (FALSE); then the tQSSA (sQSSA) model is used. |
| timespan | time points when the concentrations of products were measured. |
| products | measured concentrations of products |
| enz | initial enzyme concentrations |
| subs | initial substrate concentrations |
| K_M | true value of the Michaelis-Menten constant. |
| catal_m | prior mean of gamma prior for the catalytic constant k_{cat} . |
| catal_v | prior variance of gamma prior for the catalytic constant k_{cat} . |
| nrepeat | number of effective iteration, i.e., posterior samples. |
| jump | length of distance between sampling, i.e., thinning rate. |
| burn | length of burn-in period. |
| volume | the volume of a system. It is used to scale the product concentration. FALSE input provides automatic scaling. |

t_unit the unit of time points. It can be an arbitrary string.
 c_unit the unit of concentrations. It can be an arbitrary string.

Details

The function `catalytic_est` generates a set of Monte Carlo simulation samples from posterior distribution of the catalytic constant of enzyme kinetics model. Because the function estimates only the catalytic constant, the true value of the Michaelis-Menten constant should be given. Authors' recommendation: "Do not use this function directly. Do use the function `main_est()` to estimate the parameter so that the main function calls this function"

Value

A vector containing posterior samples of the estimated parameter: the catalytic constant.

Examples

```
## Not run:
data("timeseries_data_example")
timespan1=timeseries_data_example[,c(1,3,5,7)]
products1=timeseries_data_example[,c(2,4,6,8)]
catalytic_result <- catalytic_est(method=TRUE,timespan=timespan1,
products=products1,enz = c(4.4, 4.4, 440, 440), subs=c(4.4, 4.4, 4.4, 4.4),
K_M=44, catal_m = 1, catal_v = 1000, jump = 10, burn = 1000, nrepeat = 1000,
volume = FALSE, t_unit = "sec", c_unit = "mM")

## End(Not run)
```

| | |
|----------|---|
| main_est | <i>Main function for estimating catalytic constant k_{cat} and Michaelis-Menten (MM) constant K_M</i> |
|----------|---|

Description

The function estimates either the catalytic constant, the Michaelis-Menten constant, or both simultaneously using progress-curve data, initial enzyme concentrations, and initial substrate concentrations.

Usage

```
main_est(
  method = TRUE,
  timeseries,
  enz,
  subs,
  K_M = FALSE,
  catal = FALSE,
  K_M_init = FALSE,
```

```

std = FALSE,
tun = 2.4,
nrepeat = 1000,
jump = 10,
burn = 1000,
catal_m = 1,
catal_v = 1e+06,
K_M_m = FALSE,
K_M_v = FALSE,
volume = FALSE,
t_unit,
c_unit
)

```

Arguments

| | |
|------------|---|
| method | This determines which model, the sQSSA or tQSSA model, is used for the estimation. Specifically, the input for method is TRUE (FALSE); then the tQSSA (sQSSA) model is used. Its default value is TRUE. |
| timeseries | Data frame containing the time points and measured concentrations of products. Every two columns represent the time points when the concentrations of the products were measured and the corresponding measured concentrations. |
| enz | initial enzyme concentrations |
| subs | initial substrate concentrations |
| K_M | true value of the Michaelis-Menten constant. Specify this object if the true value is known. Its default value is FALSE. |
| catal | true value of the catalytic constant. Specify this object if the true value is known. Its default value is FALSE. |
| K_M_init | initial value of K_M constant for the Metropolis-Hastings algorithm. If the input is FALSE then it is determined by max(subs). Its default value is FALSE. |
| std | standard deviation of proposal distribution. If the input is FALSE then it is determined by using the hessian of log posterior distribution. Its default value is FALSE. |
| tun | tuning constant for the Metropolis-Hastings algorithm when std is FALSE (i.e., hessian of the log posterior distribution is used). Its default value is 2.4. |
| nrepeat | number of effective iteration, i.e., posterior samples. Its default value is 1,000. |
| jump | length of distance between sampling, i.e., thinning rate. Its default value is 10. |
| burn | length of burn-in period. Its default value is 1,000. |
| catal_m | prior mean of gamma prior for the catalytic constant k_cat. Its default value is 1. |
| catal_v | prior variance of gamma prior for the catalytic constant k_cat. Its default value is 1e+06. |
| K_M_m | prior mean of gamma prior for the Michaelis-Menten constant K_M. If the input is FALSE then it is determined by max(subs). Its default value is FALSE. |

| | |
|--------|--|
| K_M_v | prior variance of gamma prior for the Michaelis-Menten constant K_M. If the input is FALSE then it is determined by $\max(\text{subs})^2 \cdot 1000$. Its default value is FALSE. |
| volume | the volume of a system. It is used to scale the product concentration. FALSE input provides automatic scaling. Its default value is FALSE. |
| t_unit | the unit of time points. It can be an arbitrary string. |
| c_unit | the unit of concentrations. It can be an arbitrary string. |

Details

The function `main_est` generates a set of Markov Chain Monte Carlo (MCMC) simulation samples from the posterior distribution of the catalytic constant or (and) the Michaelis-Menten constant of enzyme kinetics model. Users should input initial enzyme concentrations, substrate concentrations, and progress-curve data. Prior information for both parameters can be given. The Gibbs sampling and Metropolis Hastings algorithms are used to sample the parameters. Parameters for the MCMC such as tuning parameter for proposal distribution, prior parameters, and the iteration number can be specified by users. This function use one of `catalytic_est()`, `MM_est()`, `MM_catal_est()` to generate the samples depending on parameter(s) to be estimated.

Value

A vector (or matrix) containing posterior samples of the estimated parameter(s).

Examples

```
## Not run:
data("timeseries_data_example")
result <- main_est(method=TRUE, timeseries = timeseries_data_example,
enz = c(4.4, 4.4, 440, 440), subs=c(4.4, 4.4, 4.4, 4.4), K_M_init = 1e+1,
std=1e+1, tun = 3.5, jump=10, burn=1000, nrepeat=1000,
catal_m=1, catal_v=100, K_M_m=1, K_M_v=1e+4, volume = FALSE,
t_unit = "sec", c_unit = "mM")

## End(Not run)
```

| | |
|--------------|--|
| MM_catal_est | <i>Function for estimating both of the Michaelis-Menten constant and catalytic constant simultaneously</i> |
|--------------|--|

Description

The function estimates both of the catalytic and the Michaelis-Menten constants simultaneously using progress-curve data, enzyme concentrations, and substrate concentrations.

Usage

```
MM_catal_est(
  method,
  timespan,
  products,
  enz,
  subs,
  K_M_init,
  std,
  tun,
  nrepeat,
  jump,
  burn,
  catal_m,
  catal_v,
  K_M_m,
  K_M_v,
  volume,
  t_unit,
  c_unit
)
```

Arguments

| | |
|----------|--|
| method | This determines which model, the sQSSA or tQSSA model, is used for the estimation. Specifically, the input for method is TRUE (FALSE); then the tQSSA (sQSSA) model is used. |
| timespan | time points when the concentrations of products were measured. |
| products | measured concentrations of products |
| enz | initial enzyme concentrations |
| subs | initial substrate concentrations |
| K_M_init | initial value of K_M constant for the Metropolis-Hastings algorithm. If the input is FALSE then it is determined by max(subs). |
| std | standard deviation of proposal distribution. If the input is FALSE then it is determined by using the hessian of log posterior distribution. |
| tun | tunning constant for the Metropolis-Hastings algorithm when std is FALSE (i.e., hessian of the log posterior distribution is used). |
| nrepeat | number of effective iteration, i.e., posterior samples. |
| jump | length of distance between sampling, i.e., thinning rate. |
| burn | length of burn-in period. |
| catal_m | prior mean of gamma prior for the catalytic constant k_cat. |
| catal_v | prior variance of gamma prior for the catalytic constant k_cat. |
| K_M_m | prior mean of gamma prior for the Michaelis-Menten constant K_M. If the input is FALSE then it is determined by max(subs). |

| | |
|--------|--|
| K_M_v | prior variance of gamma prior for the Michaelis-Menten constant K_M. If the input is FALSE then it is determined by $\max(\text{subs})^2 * 1000$. |
| volume | the volume of a system. It is used to scale the product concentration. FALSE input provides automatic scaling. |
| t_unit | the unit of time points. It can be an arbitrary string. |
| c_unit | the unit of concentrations. It can be an arbitrary string. |

Details

The function `MM_catal_est` generates a set of Markov Chain Monte Carlo simulation samples from the posterior distribution of K_M and catalytic constant of enzyme kinetics model. Authors' recommendation: "Do not use this function directly. Do use the function `main_est()` to estimate the parameters so that the main function calls this function"

Value

A matrix containing posterior samples of the estimated parameters: the catalytic constant and the Michaelis-Menten constant.

Examples

```
## Not run:
data("timeseries_data_example")
timespan1=timeseries_data_example[,c(1,3,5,7)]
products1=timeseries_data_example[,c(2,4,6,8)]
MM_catal_result <- MM_catal_est(method=TRUE,timespan=timespan1,
products=products1,enz = c(4.4, 4.4, 440, 440), subs=c(4.4, 4.4, 4.4, 4.4),
K_M_init = 1, catal_m=1, catal_v = 1000, K_M_m = 1, K_M_v = 100000,
std = 10, tun =3.5, nrepeat = 1000, jump = 10, burn = 1000,
volume = FALSE, t_unit = "sec", c_unit = "mM")

## End(Not run)
```

MM_est

Function for estimating the Michaelis-Menten constant

Description

The function estimates the Michaelis-Menten constant using progress-curve data, enzyme concentrations, substrate concentrations, and the catalytic constant.

Usage

```
MM_est(
  method,
  timespan,
  products,
  enz,
```

```

subs,
catal,
K_M_init,
std,
tun,
nrepeat,
jump,
burn,
K_M_m,
K_M_v,
volume,
t_unit,
c_unit
)

```

Arguments

| | |
|----------|--|
| method | This determines which model, the sQSSA or tQSSA model, is used for the estimation. Specifically, the input for method is TRUE (FALSE); then the tQSSA (sQSSA) model is used. |
| timespan | time points when the concentrations of products were measured. |
| products | measured concentrations of products |
| enz | initial enzyme concentrations |
| subs | initial substrate concentrations |
| catal | true value of the catalytic constant. |
| K_M_init | initial value of K_M constant for the Metropolis-Hastings algorithm. If the input is FALSE then it is determined by max(subs). |
| std | standard deviation of proposal distribution. If the input is FALSE then it is determined by using the hessian of log posterior distribution. |
| tun | tuning constant for the Metropolis-Hastings algorithm when std is FALSE (i.e., hessian of the log posterior distribution is used). |
| nrepeat | number of effective iteration, i.e., posterior samples. |
| jump | length of distance between sampling, i.e., thinning rate. |
| burn | length of burn-in period. |
| K_M_m | prior mean of gamma prior for the Michaelis-Menten constant K_M. If the input is FALSE then it is determined by max(subs). |
| K_M_v | prior variance of gamma prior for the Michaelis-Menten constant K_M. If the input is FALSE then it is determined by max(subs)^2*1000. |
| volume | the volume of a system. It is used to scale the product concentration. FALSE input provides automatic scaling. |
| t_unit | the unit of time points. It can be an arbitrary string. |
| c_unit | the unit of concentrations. It can be an arbitrary string. |

Details

The function `MM_est` generates a set of Markov Chain Monte Carlo simulation samples from posterior distribution of the Michaelis-Menten constant of enzyme kinetics model. Because the function estimates only the Michaelis-Menten constant the true value of the catalytic constant should be given. Authors' recommendation: "Do not use this function directly. Do use the function `main_est()` to estimate the parameter so that the main function calls this function"

Value

A vector containing posterior samples of the estimated parameter: the Michaelis-Menten constant.

Examples

```
## Not run:
data("timeseries_data_example")
timespan1=timeseries_data_example[,c(1,3,5,7)]
products1=timeseries_data_example[,c(2,4,6,8)]
MM_result <- MM_est(method=TRUE,timespan=timespan1,products=products1,
enz = c(4.4, 4.4, 440, 440), subs=c(4.4, 4.4, 4.4, 4.4), catal = 0.051,
K_M_init = 1, K_M_m = 1, K_M_v = 100000, std = 10, tun =3.5,
nrepeat = 1000, jump = 10, burn = 1000, volume = FALSE,
t_unit = "sec", c_unit = "mM")

## End(Not run)
```

timeseries_data_example

Product concentration of 101 observed time with different initial conditions

Description

An artificial data set containing the product concentration observed with the high and low enzyme concentrations. The 1st, 3rd, 5th, and 7th columns are observed times, and the 2nd, 4th, 6th, and 8th columns are product concentrations. The 2nd and 4th columns are observed with the initial enzyme concentrations of 4.4, and the 6th and 8th columns are observed with the initial enzyme concentrations of 440. The initial substrate concentrations are 4.4 for all data.

Usage

```
timeseries_data_example
```

Format

A data frame with 101 rows and 8 variables:

V1 V3 V5 V7 observed times, no unit

V2 V4 V6 V8 product concentrations, no unit

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