

# Package ‘magi’

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**Title** MAnifold-Constrained Gaussian Process Inference

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**Description**

Provides fast and accurate inference for the parameter estimation problem in Ordinary Differential Equations, including the case when there are unobserved system components. Implements the MAGI method (MAnifold-constrained Gaussian process Inference) of Yang, Wong, and Kou (2021) <[doi:10.1073/pnas.2020397118](https://doi.org/10.1073/pnas.2020397118)>.

**URL** <https://arxiv.org/abs/2203.06066>

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calCov

*Calculate stationary Gaussian process kernel*


---

**Description**

Covariance calculations for Gaussian process kernels. Currently supports matern, rbf, compact1, periodicMatern, generalMatern, and rationalQuadratic kernels. Can also return m\_phi and other additional quantities useful for ODE inference.

**Usage**

```
calCov(
  phi,
  rInput,
  signrInput,
  bandsize = NULL,
  complexity = 3,
  kerneltype = "matern",
  df,
  noiseInjection = 1e-07
)
```

**Arguments**

phi	the kernel hyper-parameters. See details for hyper-parameter specification for each kernel type.
rInput	the distance matrix between all time points s and t, i.e.,  s - t
signrInput	the sign matrix of the time differences, i.e., sign(s - t)
bandsize	size for band matrix approximation. See details.
complexity	integer value for the complexity of the kernel calculations desired: <ul style="list-style-type: none"> <li>• 0 includes C only</li> <li>• 1 additionally includes Cprime, Cdoubleprime, dCdphi</li> <li>• 2 or above additionally includes Ceigen1over, CeigenVec, Cinv, mphi, Kphi, Keigen1over, KeigenVec, Kinvg, mphiLeftHalf, dCdphiCube</li> </ul> See details for their definitions.
kerneltype	must be one of matern, rbf, compact1, periodicMatern, generalMatern, rationalQuadratic. See details for the kernel formulae.
df	degrees of freedom, for generalMatern and rationalQuadratic kernels only. Default is df=2.01 for generalMatern and df=0.01 for rationalQuadratic.
noiseInjection	a small value added to the diagonal elements of C and Kphi for numerical stability

**Details**

The covariance formulae and the hyper-parameters phi for the supported kernels are as follows. Stationary kernels have  $C(s, t) = C(r)$  where  $r = |s - t|$  is the distance between the two time points. Generally, the hyper-parameter phi[1] controls the overall variance level while phi[2] controls the bandwidth.

matern This is the simplified Matern covariance with  $df = 5/2$ :

$$C(r) = \text{phi}[1] * (1 + \sqrt{5}r/\text{phi}[2] + 5r^2/(3\text{phi}[2]^2)) * \exp(-\sqrt{5}r/\text{phi}[2])$$

rbf

$$C(r) = \text{phi}[1] * \exp(-r^2/(2\text{phi}[2]^2))$$

compact1

$$C(r) = \text{phi}[1] * \max(1 - r/\text{phi}[2], 0)^4 * (4r/\text{phi}[2] + 1)$$

periodicMatern Define  $r' = |\sin(r\pi/\text{phi}[3]) * 2|$ . Then the covariance is given by  $C(r')$  using the Matern formula.

generalMatern

$$C(r) = \text{phi}[1] * 2^{(1-df)}/\Gamma(df) * (\sqrt{(2.0*df)*r}/\text{phi}[2])^d * \text{besselK}(\sqrt{(2.0*df)*r}/\text{phi}[2], df)$$

where `besselK` is the modified Bessel function of the second kind.

rationalQuadratic

$$C(r) = \text{phi}[1] * (1 + r^2/(2df\text{phi}[2]^2))^{-(df)}$$

The kernel calculations available and their definitions are as follows:

**C** The covariance matrix corresponding to the distance matrix `rInput`.

**Cprime** The cross-covariance matrix  $dC(s, t)/ds$ .

**Cdoubleprime** The cross-covariance matrix  $d^2C(s, t)/dsdt$ .

**dCdphi** A list with the matrices  $dC/dphi$  for each element of `phi`.

**Ceigenlover** The reciprocals of the eigenvalues of `C`.

**CeigenVec** Matrix of eigenvectors of `C`.

**Cinv** The inverse of `C`.

**mphi** The matrix `Cprime * Cinv`.

**Kphi** The matrix `Cdoubleprime - Cprime * Kinv * t(Cprime)`.

**Keigenlover** The reciprocals of the eigenvalues of `Kphi`.

**Kinv** The inverse of `Kphi`.

**mphiLeftHalf** The matrix `Cprime * CeigenVec`.

**dCdphiCube**  $dC/dphi$  as a 3-D array, with the third dimension corresponding to the elements of `phi`.

If `bandsize` is a positive integer, additionally `CinvBand`, `mphiBand`, and `KinvBand` are provided in the return list, which are band matrix approximations to `Cinv`, `mphi`, and `Kinv` with the specified `bandsize`.

## Value

A list containing the kernel calculations included by the value of `complexity`.

## Examples

```
foo <- outer(0:40, t(0:40), '-')[, 1, ]
r <- abs(foo)
signr <- -sign(foo)
calCov(c(0.2, 2), r, signr, bandsize = 20, kerneltype = "generalMatern", df = 2.01)
```

---

FNdat	<i>Dataset of noisy observations from the FitzHugh-Nagumo (FN) equations</i>
-------	--

---

## Description

The classic FN equations model the spike potentials of neurons, where system components  $V$  and  $R$  are the voltage and recovery variables, respectively.

$V$  and  $R$  are governed by the following differential equations:

$$\frac{dV}{dt} = c\left(V - \frac{V^3}{3} + R\right)$$

$$\frac{dR}{dt} = -\frac{1}{c}(V - a + bR)$$

where  $\theta = (a, b, c)$  are system parameters. This dataset was generated by first numerically solving these ODEs from  $t = 0$  to  $t = 20$ , with initial conditions  $V(0) = -1$  and  $R(0) = 1$  and parameters  $\theta = (0.2, 0.2, 3)$ . The system components were taken to be measured at 28 observation time points (as indicated in `time` column) with additive Gaussian noise (standard deviation 0.2).

### Usage

```
data(FNdat)
```

### Format

A data frame with 28 rows and 3 columns (`time`, `V`, `R`).

### References

FitzHugh, R (1961). Impulses and Physiological States in Theoretical Models of Nerve Membrane. *Biophysical Journal*, 1(6), 445–466.

---

 fnmodelODE

*The FitzHugh-Nagumo (FN) equations*


---

### Description

The classic FN equations model the spike potentials of neurons, where system components  $X = (V, R)$  represent the voltage and recovery variables, respectively.

$V$  and  $R$  are governed by the following differential equations:

$$\frac{dV}{dt} = c(V - \frac{V^3}{3} + R)$$

$$\frac{dR}{dt} = -\frac{1}{c}(V - a + bR)$$

where  $\theta = (a, b, c)$  are system parameters.

### Usage

```
fnmodelODE(theta, x, tvec)
```

```
fnmodelDx(theta, x, tvec)
```

```
fnmodelDtheta(theta, x, tvec)
```

**Arguments**

theta	vector of parameters.
x	matrix of system states (one per column) at the time points in tvec.
tvec	vector of time points

**Value**

fnmodelODE returns an array with the values of the derivatives  $\dot{X}$ .

fnmodelDx returns a 3-D array with the values of the gradients with respect to  $X$ .

fnmodelDtheta returns a 3-D array with the values of the gradients with respect to  $\theta$ .

**References**

FitzHugh, R (1961). Impulses and Physiological States in Theoretical Models of Nerve Membrane. *Biophysical Journal*, 1(6), 445–466.

**Examples**

```
theta <- c(0.2, 0.2, 3)
x <- matrix(1:10, nrow = 5, ncol = 2)
tvec <- 1:5

fnmodelODE(theta, x, tvec)
```

---

gpcov

---

*Conditional covariance of Gaussian process given observations*


---

**Description**

Compute the conditional covariance of a Gaussian process, given a vector of observations, hyper-parameters phi, and noise standard deviation sigma.

**Usage**

```
gpcov(yobs, tvec, tnew, phi, sigma, kerneltype = "generalMatern")
```

**Arguments**

yobs	vector of observations
tvec	vector of time points corresponding to observations
tnew	vector of time points at which the conditional covariance should be computed
phi	vector of hyper-parameters for the covariance kernel (kerneltype)
sigma	the noise level (if known). By default, both phi and sigma are estimated. If a value for sigma is supplied, then sigma is held fixed at the supplied value and only phi is estimated.
kerneltype	the covariance kernel, types matern, rbf, compact1, periodicMatern, generalMatern are supported. See <a href="#">calCov</a> for their definitions.

**Value**

The conditional covariance matrix for the GP evaluated at the time points in tnew.

**Examples**

```
# Load Fitzhugh-Nagumo dataset
data(FNdat)

tnew <- seq(15, 20, by = 0.5)

# GP covariance of V component at time points in tnew given observations
gpcov(FNdat$V, FNdat$time, tnew, c(2.3, 1.2), 0.2)
```

---

gpmean

*Conditional mean of Gaussian process given observations*


---

**Description**

Compute the conditional mean of a Gaussian process (and optionally, its derivative), given a vector of observations, hyper-parameters phi, and noise standard deviation sigma.

**Usage**

```
gpmean(
  yobs,
  tvec,
  tnew,
  phi,
  sigma,
  kerneltype = "generalMatern",
  deriv = FALSE
)
```

**Arguments**

yobs	vector of observations
tvec	vector of time points corresponding to observations
tnew	vector of time points at which the conditional mean should be computed
phi	vector of hyper-parameters for the covariance kernel (kerneltype)
sigma	the noise level (if known). By default, both phi and sigma are estimated. If a value for sigma is supplied, then sigma is held fixed at the supplied value and only phi is estimated.
kerneltype	the covariance kernel, types matern, rbf, compact1, periodicMatern, generalMatern are supported. See <a href="#">calCov</a> for their definitions.
deriv	logical; if true, the conditional mean of the GP's derivative is also computed

**Value**

A vector with the values of the conditional mean function evaluated at the time points in `tnew`. If `deriv = TRUE`, returned with an additional attribute `deriv` that contains the values of the conditional mean of the GP derivative evaluated at the time points in `tnew`.

**Examples**

```
# Load Fitzhugh-Nagumo dataset
data(FNdat)

tnew <- seq(0, 20, by = 0.5)

# GP mean of V component at time points in tnew given observations
gpmean(FNdat$V, FNdat$time, tnew, c(2.3, 1.2), 0.2)
```

---

gpsmoothing

*Gaussian process smoothing*

---

**Description**

Estimate hyper-parameters `phi` and noise standard deviation `sigma` for a vector of observations using Gaussian process smoothing.

**Usage**

```
gpsmoothing(yobs, tvec, kerneltype = "generalMatern", sigma = NULL)
```

**Arguments**

<code>yobs</code>	vector of observations
<code>tvec</code>	vector of time points corresponding to observations
<code>kerneltype</code>	the covariance kernel, types <code>matern</code> , <code>rbf</code> , <code>compact1</code> , <code>periodicMatern</code> , <code>generalMatern</code> are supported. See <a href="#">calCov</a> for their definitions.
<code>sigma</code>	the noise level (if known). By default, both <code>phi</code> and <code>sigma</code> are estimated. If a value for <code>sigma</code> is supplied, then <code>sigma</code> is held fixed at the supplied value and only <code>phi</code> is estimated.

**Value**

A list containing the elements `phi` and `sigma` with their estimated values.



**Examples**

```
# Sample data and observation times
tvec <- seq(0, 20, by = 0.5)
y <- c(-1.16, -0.18, 1.57, 1.99, 1.95, 1.85, 1.49, 1.58, 1.47, 0.96,
0.75, 0.22, -1.34, -1.72, -2.11, -1.56, -1.51, -1.29, -1.22,
-0.36, 1.78, 2.36, 1.78, 1.8, 1.76, 1.4, 1.02, 1.28, 1.21, 0.04,
-1.35, -2.1, -1.9, -1.49, -1.55, -1.35, -0.98, -0.34, 1.9, 1.99, 1.84)

gpsmoothing(y, tvec)
```

---

gpsmoothlik

---

*Marginal log-likelihood for Gaussian process smoothing*


---

**Description**

Marginal log-likelihood and gradient as a function of GP hyper-parameters  $\phi$  and observation noise standard deviation  $\sigma$ . For use in Gaussian process smoothing where values of  $\phi$  and  $\sigma$  may be optimized.

**Usage**

```
gpsmoothlik(phisig, yobs, rInput, kerneltype = "generalMatern")
```

**Arguments**

phisig	vector containing GP hyper-parameters $\phi$ and observation noise SD $\sigma$ . See <a href="#">calCov</a> for the definitions of the hyper-parameters.
yobs	vector of observations
rInput	distance matrix between all time points of yobs
kerneltype	the covariance kernel, types matern, rbf, compact1, periodicMatern, generalMatern are supported. See <a href="#">calCov</a> for their definitions.

**Value**

A list with elements value and grad, which are the log-likelihood value and gradient with respect to phisig, respectively.

**Examples**

```
# Suppose phi[1] = 0.5, phi[2] = 3, sigma = 0.1
gpsmoothlik(c(0.5, 3, 0.1), rnorm(10), abs(outer(0:9, t(0:9), '-')[, 1, ]))
```

hes1modelODE

*Hes1 equations: oscillation of mRNA and protein levels***Description**

The Hes1 equations model the oscillatory cycles of protein and messenger ribonucleic acid (mRNA) levels in cultured cells. The system components  $X = (P, M, H)$  represent the concentrations of protein, mRNA, and the Hes1-interacting factor that provides a negative feedback loop.

$P$ ,  $M$ , and  $H$  are governed by the following differential equations:

$$\begin{aligned}\frac{dP}{dt} &= -aPH + bM - cP \\ \frac{dM}{dt} &= -d_M M + \frac{e}{1 + P^2} \\ \frac{dH}{dt} &= -aPH + \frac{f}{1 + P^2} - gH\end{aligned}$$

where  $\theta = (a, b, c, d_M, e, f, g)$  are system parameters.

**Usage**

```
hes1modelODE(theta, x, tvec)
```

```
hes1modelDx(theta, x, tvec)
```

```
hes1modelDtheta(theta, x, tvec)
```

```
hes1logmodelODE(theta, x, tvec)
```

```
hes1logmodelDx(theta, x, tvec)
```

```
hes1logmodelDtheta(theta, x, tvec)
```

**Arguments**

theta	vector of parameters.
x	matrix of system states (one per column) at the time points in tvec.
tvec	vector of time points

**Value**

hes1modelODE returns an array with the values of the derivatives  $\dot{X}$ .

hes1modelDx returns a 3-D array with the values of the gradients with respect to  $X$ .

hes1modelDtheta returns a 3-D array with the values of the gradients with respect to  $\theta$ .

hes1logmodelODE, hes1logmodelDx, and hes1logmodelDtheta are the log-transformed versions of hes1modelODE, hes1modelDx, and hes1modelDtheta, respectively.

## References

Hirata H, Yoshiura S, Ohtsuka T, Bessho Y, Harada T, Yoshikawa K, Kageyama R (2002). Oscillatory Expression of the bHLH Factor Hes1 Regulated by a Negative Feedback Loop. *Science*, 298(5594), 840–843.

## Examples

```
theta <- c(0.022, 0.3, 0.031, 0.028, 0.5, 20, 0.3)
x <- matrix(1:15, nrow = 5, ncol = 3)
tvec <- 1:5

hes1modelODE(theta, x, tvec)
```

---

is.magioutput	<i>MagiSolver</i> output (magioutput) object
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---

## Description

Check for and create a magioutput object

## Usage

```
is.magioutput(object)

magioutput(...)
```

## Arguments

object	an R object
...	arguments required to create a magioutput object. See details.

## Details

Using the core [MagiSolver](#) function returns a magioutput object as output, which is a list that contains the following elements:

- theta matrix of MCMC samples for the system parameters  $\theta$ , after burn-in.
- xsampled array of MCMC samples for the system trajectories at each discretization time point, after burn-in.
- sigma matrix of MCMC samples for the observation noise SDs  $\sigma$ , after burn-in.
- phi matrix of estimated GP hyper-parameters, one column for each system component.
- lp vector of log-posterior values at each MCMC iteration, after burn-in.
- y, tvec, odeModel from the inputs to MagiSolver.

Printing a magioutput object displays a brief summary of the settings used for the MagiSolver run. The summary method for a magioutput object prints a table of parameter estimates, see [summary.magioutput](#) for more details. Plotting a magioutput object by default shows the inferred trajectories for each component, see [plot.magioutput](#) for more details.

**Value**

logical. Is the input a magioutput object?

**Examples**

```
# Set up odeModel list for the Fitzhugh-Nagumo equations
fnmodel <- list(
  fOde = fnmodelODE,
  fOdeDx = fnmodelDx,
  fOdeDtheta = fnmodelDtheta,
  thetaLowerBound = c(0, 0, 0),
  thetaUpperBound = c(Inf, Inf, Inf)
)

# Example FN data
data(FNdat)

# Create magioutput from a short MagiSolver run (demo only, more iterations needed for convergence)
result <- MagiSolver(FNdat, fnmodel, control = list(nstepsHmc = 5, niterHmc = 50))

is.magioutput(result)
```

---

magi

magi: *MANifold-Constrained Gaussian Process Inference*

---

**Description**

magi is a package that provides fast and accurate inference for the parameter estimation problem in Ordinary Differential Equations, including the case when there are unobserved system components. In the references below, please see Yang, Wong, and Kou (2021) for details of the MAGI method (MANifold-constrained Gaussian process Inference), and Wong, Yang, and Kou (2022) for a detailed user guide.

**References**

- Yang, S., Wong, S. W. K., & Kou, S. C. (2021). Inference of Dynamic Systems from Noisy and Sparse Data via Manifold-constrained Gaussian Processes. *Proceedings of the National Academy of Sciences*, 118 (15), e2020397118. [doi:10.1073/pnas.2020397118](https://doi.org/10.1073/pnas.2020397118)
- Wong, S. W. K., Yang, S., & Kou, S. C. (2022). MAGI: A Package for Inference of Dynamic Systems from Noisy and Sparse Data via Manifold-constrained Gaussian Processes. <https://arxiv.org/abs/2203.06066>

---

MagiPosterior	<i>MAGI posterior density</i>
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---

**Description**

Computes the MAGI log-posterior value and gradient for an ODE model with the given inputs: the observations  $Y$ , the latent system trajectories  $X$ , the parameters  $\theta$ , the noise standard deviations  $\sigma$ , and covariance kernels.

**Usage**

```
MagiPosterior(
  y,
  xlatent,
  theta,
  sigma,
  covAllDimInput,
  odeModel,
  priorTemperatureInput = 1,
  useBand = FALSE
)
```

**Arguments**

y	data matrix of observations
xlatent	matrix of system trajectory values
theta	vector of parameter values $\theta$
sigma	vector of observation noise for each system component
covAllDimInput	list of covariance kernel objects for each system component. Covariance calculations may be carried out with <a href="#">calCov</a> .
odeModel	list of ODE functions and inputs. See details.
priorTemperatureInput	vector of tempering factors for the GP prior, derivatives, and observations, in that order. Controls the influence of the GP prior relative to the likelihood. Recommended values: the total number of observations divided by the total number of discretization points for the GP prior and derivatives, and 1 for the observations.
useBand	logical: should the band matrix approximation be used? If TRUE, covAllDimInput must include CinvBand, mphiBand, and KinvBand as computed by <a href="#">calCov</a> .

**Value**

A list with elements value for the value of the log-posterior density and grad for its gradient.

**Examples**

```

# Trajectories from the Fitzhugh-Nagumo equations
tvec <- seq(0, 20, 2)
Vtrue <- c(-1, 1.91, 1.38, -1.32, -1.5, 1.73, 1.66, 0.89, -1.82, -0.93, 1.89)
Rtrue <- c(1, 0.33, -0.62, -0.82, 0.5, 0.94, -0.22, -0.9, -0.08, 0.95, 0.3)

# Noisy observations
Vobs <- Vtrue + rnorm(length(tvec), sd = 0.05)
Robs <- Rtrue + rnorm(length(tvec), sd = 0.1)

# Prepare distance matrix for covariance kernel calculation
foo <- outer(tvec, t(tvec), '-')[, 1, ]
r <- abs(foo)
r2 <- r^2
signr <- -sign(foo)

# Choose some hyperparameter values to illustrate
rphi <- c(0.95, 3.27)
vphi <- c(1.98, 1.12)
phiTest <- cbind(vphi, rphi)

# Covariance computations
curCovV <- calCov(phiTest[,1], r, signr, kerneltype = "generalMatern")
curCovR <- calCov(phiTest[,2], r, signr, kerneltype = "generalMatern")

# Y and X inputs to MagiPosterior
yInput <- data.matrix(cbind(Vobs, Robs))
xlatentTest <- data.matrix(cbind(Vtrue, Rtrue))

# Create odeModel list for FN equations
fnmodel <- list(
  fOde = fnmodelODE,
  fOdeDx = fnmodelDx,
  fOdeDtheta = fnmodelDtheta,
  thetaLowerBound = c(0, 0, 0),
  thetaUpperBound = c(Inf, Inf, Inf)
)

MagiPosterior(yInput, xlatentTest, theta = c(0.2, 0.2, 3), sigma = c(0.05, 0.1),
  list(curCovV, curCovR), fnmodel)

```

**Description**

Core function of the MAGI method for inferring the parameters and trajectories of dynamic systems governed by ordinary differential equations.

**Usage**

```
MagiSolver(y, odeModel, tvec, control = list())
```

**Arguments**

<code>y</code>	data matrix of observations
<code>odeModel</code>	list of ODE functions and inputs. See details.
<code>tvec</code>	vector of discretization time points corresponding to rows of <code>y</code> . If missing, <code>MagiSolver</code> will use the column named 'time' in <code>y</code> .
<code>control</code>	list of control variables, which may include 'sigma', 'phi', 'theta', 'xInit', 'mu', 'dotmu', 'priorTemperature', 'niterHmc', 'nstepsHmc', 'burninRatio', 'stepSizeFactor', 'bandSize', 'useFixedSigma', 'kerneltype', 'skipMissingComponentOptimization', 'positiveSystem', 'verbose'. See details.

**Details**

The data matrix `y` has a column for each system component, and optionally a column 'time' with the discretization time points. If the column 'time' is not provided in `y`, a vector of time points must be provided via the `tvec` argument. The rows of `y` correspond to the discretization set  $I$  at which the GP is constrained to the derivatives of the ODE system. To set the desired discretization level for inference, use [setDiscretization](#) to prepare the data matrix for input into `MagiSolver`. Missing observations are indicated with NA or NaN.

The list `odeModel` is used for specification of the ODE system and its parameters. It must include five elements:

`fOde` function that computes the ODEs, specified with the form  $f(\theta, x, tvec)$ . `fOde` should return a matrix where columns correspond to the system components of `x`, see examples.

`fOdeDx` function that computes the gradients of the ODEs with respect to the system components. `fOdeDx` should return a 3-D array, where the slice  $[, i, j]$  is the partial derivative of the ODE for the  $j$ -th system component with respect to the  $i$ -th system component, see examples.

`fOdeDtheta` function that computes the gradients of the ODEs with respect to the parameters  $\theta$ . `fOdeDtheta` should return a 3-D array, where the slice  $[, i, j]$  is the partial derivative of the ODE for the  $j$ -th system component with respect to the  $i$ -th parameter in  $\theta$ , see examples.

`thetaLowerBound` a vector indicating the lower bounds of each parameter in  $\theta$ .

`thetaUpperBound` a vector indicating the upper bounds of each parameter in  $\theta$ .

Additional control variables can be supplied to `MagiSolver` via the optional list `control`, which may include the following:

`sigma` a vector of noise levels (observation noise standard deviations)  $\sigma$  for each component, at which to initialize MCMC sampling. By default, `MagiSolver` computes starting values for `sigma` via Gaussian process (GP) smoothing. If the noise levels are known, specify `sigma` together with `useFixedSigma = TRUE`.

`phi` a matrix of GP hyper-parameters for each component, with rows for the kernel hyper-parameters and columns for the system components. By default, `MagiSolver` estimates `phi` via an optimization routine.

- `theta` a vector of starting values for the parameters  $\theta$ , at which to initialize MCMC sampling. By default, MagiSolver uses an optimization routine to obtain starting values.
- `xInit` a matrix of values for the system trajectories of the same dimension as `y`, at which to initialize MCMC sampling. Default is linear interpolation between the observed (non-missing) values of `y` and an optimization routine for entirely unobserved components of `y`.
- `mu` a matrix of values for the mean function of the GP prior, of the same dimension as `y`. Default is a zero mean function.
- `dotmu` a matrix of values for the derivatives of the GP prior mean function, of the same dimension as `y`. Default is zero.
- `priorTemperature` the tempering factor by which to divide the contribution of the GP prior, to control the influence of the GP prior relative to the likelihood. Default is the total number of observations divided by the total number of discretization points.
- `niterHmc` MCMC sampling from the posterior is carried out via the Hamiltonian Monte Carlo (HMC) algorithm. `niterHmc` specifies the number of HMC iterations to run. Default is 20000 HMC iterations.
- `nstepsHmc` the number of leapfrog steps per HMC iteration. Default is 200.
- `burninRatio` the proportion of HMC iterations to be discarded as burn-in. Default is 0.5, which discards the first half of the MCMC samples.
- `stepSizeFactor` initial leapfrog step size factor for HMC. Can be specified as a scalar (applied to all posterior dimensions) or a vector (with length corresponding to the dimension of the posterior). Default is 0.01, and the leapfrog step size is automatically tuned during burn-in to achieve an acceptance rate between 60-90%.
- `bandSize` a band matrix approximation is used to speed up matrix operations, with default band size 20. Can be increased if MagiSolver returns an error indicating numerical instability.
- `useFixedSigma` logical, set to TRUE if `sigma` is known. If `useFixedSigma = TRUE`, the known values of  $\sigma$  must be supplied via the `sigma` control variable. Default is FALSE.
- `kerneltype` the GP covariance kernel, `generalMatern` is the default and recommended choice. Other available choices are `matern`, `rbf`, `compact1`, `periodicMatern`. See [calCov](#) for their definitions.
- `skipMissingComponentOptimization` logical, set to TRUE to skip automatic optimization for missing components. If `skipMissingComponentOptimization = TRUE`, values for `xInit` and `phi` must be supplied for all system components. Default is FALSE.
- `positiveSystem` logical, set to TRUE if the system cannot be negative. Default is FALSE.
- `verbose` logical, set to TRUE to output diagnostic and progress messages to the console. Default is FALSE.

## Value

MagiSolver returns an object of class `magioutput` which contains the following elements:

- `theta` matrix of MCMC samples for the system parameters  $\theta$ , after burn-in.
- `xsampled` array of MCMC samples for the system trajectories at each discretization time point, after burn-in.
- `sigma` matrix of MCMC samples for the observation noise SDs  $\sigma$ , after burn-in.



phi matrix of estimated GP hyper-parameters, one column for each system component.  
 lp vector of log-posterior values at each MCMC iteration, after burn-in.  
 y, tvec, odeModel from the inputs to MagiSolver.

## References

Shihao Yang, Samuel WK Wong, SC Kou (2021). Inference of Dynamic Systems from Noisy and Sparse Data via Manifold-constrained Gaussian Processes. *Proceedings of the National Academy of Sciences*, 118 (15), e2020397118.

## Examples

```
# Set up odeModel list for the Fitzhugh-Nagumo equations
fnmodel <- list(
  fOde = fnmodelODE,
  fOdeDx = fnmodelDx,
  fOdeDtheta = fnmodelDtheta,
  thetaLowerBound = c(0, 0, 0),
  thetaUpperBound = c(Inf, Inf, Inf)
)

# Example noisy data observed from the FN system
data(FNdat)

# Set discretization for a total of 81 equally-spaced time points from 0 to 20
yinput <- setDiscretization(FNdat, by = 0.25)

# Run MagiSolver
# Short sampler run for demo only, more iterations needed for convergence
MagiSolver(yinput, fnmodel, control = list(nstepsHmc = 5, niterHmc = 101))

# Use 3000 HMC iterations with 100 leapfrog steps per iteration
FNres <- MagiSolver(yinput, fnmodel, control = list(nstepsHmc = 100, niterHmc = 3000))
# Summary of parameter estimates
summary(FNres)
# Plot of inferred trajectories
plot(FNres, comp.names = c("V", "R"), xlab = "Time", ylab = "Level")
```

---

plot.magioutput

*Generate plots from magioutput object*

---

## Description

Plots inferred system trajectories or diagnostic traceplots from the output of MagiSolver

**Usage**

```
## S3 method for class 'magioutput'
plot(
  x,
  type = "traj",
  obs = TRUE,
  ci = TRUE,
  ci.col = "skyblue",
  comp.names,
  par.names,
  est = "mean",
  lower = 0.025,
  upper = 0.975,
  sigma = FALSE,
  lp = TRUE,
  nplotcol = 3,
  ...
)
```

**Arguments**

x	a magioutput object.
type	string; the default type = "traj" plots inferred trajectories, while setting type = "trace" generates diagnostic traceplots for the MCMC samples of the parameters and log-posterior values.
obs	logical; if true, points will be added on the plots for the observations when type = "traj".
ci	logical; if true, credible bands/intervals will be added to the plots.
ci.col	string; color to use for credible bands.
comp.names	vector of system component names, when type = "traj". If provided, should be the same length as the number of system components in $X$ .
par.names	vector of parameter names, when type = "trace". If provided, should be the same length as the number of parameters in $\theta$ , or the combined length of $\theta$ and $\sigma$ when sigma = TRUE.
est	string specifying the posterior quantity to plot as the estimate. Can be "mean", "median", "mode", or "none". Default is "mean", which plots the posterior mean of the MCMC samples.
lower	the lower quantile of the credible band/interval, default is 0.025. Only used if ci = TRUE.
upper	the upper quantile of the credible band/interval, default is 0.975. Only used if ci = TRUE.
sigma	logical; if true, the noise levels $\sigma$ will be included in the traceplots when type = "trace".
lp	logical; if true, the values of the log-posterior will be included in the traceplots when type = "trace".

nplotcol        the number of subplots per row.  
 ...            additional arguments to plot.

### Details

Plots the inferred system trajectories (when `type = "traj"`) or diagnostic traceplots of the parameters and log-posterior (when `type = "trace"`) from the MCMC samples. By default, the posterior mean is treated as the estimate of the trajectories and parameters (`est = "mean"`). Alternatives are the posterior median (`est = "median"`, taken component-wise) and the posterior mode (`est = "mode"`, approximated by the MCMC sample with the highest log-posterior value).

The default `type = "traj"` produces plots of the inferred trajectories and credible bands from the MCMC samples, one subplot for each system component. By default, `lower = 0.025` and `upper = 0.975` produces a central 95% credible band when `ci = TRUE`. Adding the observed data points (`obs = TRUE`) can provide a visual assessment of the inferred trajectories.

Setting `type = "trace"` generates diagnostic traceplots for the MCMC samples of the system parameters and the values of the log-posterior, which is a useful tool for informally assessing convergence. In this case, the `est` and `ci` options add horizontal lines to the plots that indicate the estimate (in red) and credible interval (in green) for each parameter.

### Examples

```
# Set up odeModel list for the Fitzhugh-Nagumo equations
fnmodel <- list(
  fOde = fnmodelODE,
  fOdeDx = fnmodelDx,
  fOdeDtheta = fnmodelDtheta,
  thetaLowerBound = c(0, 0, 0),
  thetaUpperBound = c(Inf, Inf, Inf)
)

# Example FN data
data(FNdat)
y <- setDiscretization(FNdat, by = 0.25)

# Create magioutput from a short MagiSolver run (demo only, more iterations needed for convergence)
result <- MagiSolver(y, fnmodel, control = list(nstepsHmc = 20, niterHmc = 500))

# Inferred trajectories
plot(result, comp.names = c("V", "R"), xlab = "Time", ylab = "Level")

# Parameter trace plots
plot(result, type = "trace", par.names = c("a", "b", "c", "sigmaV", "sigmaR"), sigma = TRUE)
```

## Description

The protein transduction equations model a biochemical reaction involving a signaling protein that degrades over time. The system components  $X = (S, S_d, R, S_R, R_{pp})$  represent the levels of signaling protein, its degraded form, inactive state of  $R$ ,  $S - R$  complex, and activated state of  $R$ .

$S, S_d, R, S_R$  and  $R_{pp}$  are governed by the following differential equations:

$$\begin{aligned}\frac{dS}{dt} &= -k_1 \cdot S - k_2 \cdot S \cdot R + k_3 \cdot S_R \\ \frac{dS_d}{dt} &= k_1 \cdot S \\ \frac{dR}{dt} &= -k_2 \cdot S \cdot R + k_3 \cdot S_R + \frac{V \cdot R_{pp}}{K_m + R_{pp}} \\ \frac{dS_R}{dt} &= k_2 \cdot S \cdot R - k_3 \cdot S_R - k_4 \cdot S_R \\ \frac{dR_{pp}}{dt} &= k_4 \cdot S_R - \frac{V \cdot R_{pp}}{K_m + R_{pp}}\end{aligned}$$

where  $\theta = (k_1, k_2, k_3, k_4, V, K_m)$  are system parameters.

## Usage

`ptransmodelODE(theta, x, tvec)`

`ptransmodelDx(theta, x, tvec)`

`ptransmodelDtheta(theta, x, tvec)`

## Arguments

<code>theta</code>	vector of parameters.
<code>x</code>	matrix of system states (one per column) at the time points in <code>tvec</code> .
<code>tvec</code>	vector of time points

## Value

`ptransmodelODE` returns an array with the values of the derivatives  $\dot{X}$ .

`ptransmodelDx` returns a 3-D array with the values of the gradients with respect to  $X$ .

`ptransmodelDtheta` returns a 3-D array with the values of the gradients with respect to  $\theta$ .

## References

Vyshemirsky, V., & Girolami, M. A. (2008). Bayesian Ranking of Biochemical System Models. *Bioinformatics*, 24(6), 833-839.

**Examples**

```
theta <- c(0.07, 0.6, 0.05, 0.3, 0.017, 0.3)
x <- matrix(1:25, nrow = 5, ncol = 5)
tvec <- 1:5

ptransmodelODE(theta, x, tvec)
```

---

setDiscretization      *Set discretization level*

---

**Description**

Set the discretization level of a data matrix for input to [MagiSolver](#), by inserting time points where the GP is constrained to the derivatives of the ODE system.

**Usage**

```
setDiscretization(dat, level, by)
```

**Arguments**

dat	data matrix. Must include a column with name 'time'.
level	discretization level (a positive integer). $2^{\text{level}} - 1$ equally-spaced time points will be inserted between each row of dat.
by	discretization interval. As an alternative to level, time points will be inserted (as needed) to form an equally-spaced discretization set from the first to last observations of dat, with interval by between successive discretization points. This can be useful when the time points in dat are unevenly spaced.

**Details**

Specify the desired discretization using level or by.

**Value**

Returns a data matrix with the same columns as dat, with rows added for the inserted discretization time points.

**Examples**

```
dat <- data.frame(time = 0:10, x = rnorm(11))
setDiscretization(dat, level = 2)
setDiscretization(dat, by = 0.2)
```

---

summary.magioutput      *Summary of parameter estimates from magioutput object*

---

## Description

Computes a summary table of parameter estimates from the output of MagiSolver

## Usage

```
## S3 method for class 'magioutput'
summary(
  object,
  sigma = FALSE,
  par.names,
  est = "mean",
  lower = 0.025,
  upper = 0.975,
  digits = 3,
  ...
)
```

## Arguments

object	a magioutput object.
sigma	logical; if true, the noise levels $\sigma$ will be included in the summary.
par.names	vector of parameter names for the summary table. If provided, should be the same length as the number of parameters in $\theta$ , or the combined length of $\theta$ and $\sigma$ when <code>sigma = TRUE</code> .
est	string specifying the posterior quantity to treat as the estimate. Default is <code>est = "mean"</code> , which treats the posterior mean as the estimate. Alternatives are the posterior median ( <code>est = "median"</code> , taken component-wise) and the posterior mode ( <code>est = "mode"</code> , approximated by the MCMC sample with the highest log-posterior value).
lower	the lower quantile of the credible interval, default is 0.025.
upper	the upper quantile of the credible interval, default is 0.975.
digits	integer; the number of significant digits to print.
...	additional arguments affecting the summary produced.

## Details

Computes parameter estimates and credible intervals from the MCMC samples. By default, the posterior mean is treated as the parameter estimate, and `lower = 0.025` and `upper = 0.975` produces a central 95% credible interval.

**Value**

Returns a matrix where rows display the estimate, lower credible limit, and upper credible limit of each parameter.

**Examples**

```
# Set up odeModel list for the Fitzhugh–Nagumo equations
fnmodel <- list(
  fOde = fnmodelODE,
  fOdeDx = fnmodelDx,
  fOdeDtheta = fnmodelDtheta,
  thetaLowerBound = c(0, 0, 0),
  thetaUpperBound = c(Inf, Inf, Inf)
)

# Example FN data
data(FNdat)

# Create magioutput from a short MagiSolver run (demo only, more iterations needed for convergence)
result <- MagiSolver(FNdat, fnmodel, control = list(nstepsHmc = 5, niterHmc = 100))

summary(result, sigma = TRUE, par.names = c("a", "b", "c", "sigmaV", "sigmaR"))
```

---

testDynamicalModel      *Test dynamic system model specification*

---

**Description**

Given functions for the ODE and its gradients (with respect to the system components and parameters), verify the correctness of the gradients using numerical differentiation.

**Usage**

```
testDynamicalModel(modelODE, modelDx, modelDtheta, modelName, x, theta, tvec)
```

**Arguments**

modelODE	function that computes the ODEs, specified with the form $f(\theta, x, tvec)$ . See examples.
modelDx	function that computes the gradients of the ODEs with respect to the system components. See examples.
modelDtheta	function that computes the gradients of the ODEs with respect to the parameters $\theta$ . See examples.
modelName	string giving a name for the model
x	data matrix of system values, one column for each component, at which to test the gradients
theta	vector of parameter values for $\theta$ , at which to test the gradients
tvec	vector of time points corresponding to the rows of x

**Details**

Calls `test_that` to test equality of the analytic and numeric gradients.

**Value**

A list with elements `testDx` and `testDtheta`, each with value `TRUE` if the corresponding gradient check passed and `FALSE` if not.

**Examples**

```
# ODE system and gradients for Fitzhugh-Nagumo equations: fnmodelODE, fnmodelDx, fnmodelDtheta

# Example of incorrect gradient with respect to parameters theta
fnmodelDthetaWrong <- function(theta, x, tvec) {
  resultDtheta <- array(0, c(nrow(x), length(theta), ncol(x)))

  V = x[, 1]
  R = x[, 2]

  resultDtheta[, 3, 1] = V - V^3 / 3.0 - R

  resultDtheta[, 1, 2] = 1.0 / theta[3]
  resultDtheta[, 2, 2] = -R / theta[3]
  resultDtheta[, 3, 2] = 1.0 / (theta[3]^2) * (V - theta[1] + theta[2] * R)

  resultDtheta
}

# Sample data for testing gradient correctness
data(FNdat)

# Correct gradients
testDynamicalModel(fnmodelODE, fnmodelDx, fnmodelDtheta,
  "FN equations", FNdat[, c("V", "R")], c(.5, .6, 2), FNdat$time)

# Incorrect theta gradient (test fails)
testDynamicalModel(fnmodelODE, fnmodelDx, fnmodelDthetaWrong,
  "FN equations", FNdat[, c("V", "R")], c(.5, .6, 2), FNdat$time)
```



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