Package 'KATforDCEMRI'

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Type Package

Title Kinetic Analysis and Visualization of DCE-MRI Data

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Depends R (>= 2.11.0)

Imports locfit, R.matlab, matlab

Description Provides kinetic analysis of Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) data. Includes tools for fitting the Tofts (described in Tofts, Kermode (1991) <DOI:10.1002/mrm.1910170208>) and extended Tofts (described in Tofts et al. (1999) <https://www.ncbi.nlm.nih.gov/pubmed/10508281>) mathematical models to dynamic (signal vs. time) data associated with each voxel of an image and a Graphical User Inferface (GUI) for visualization and exploration of fitted model parameters over the volume of the image.

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LazyLoad yes

LazyData yes

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R topics documented:

`dcemri.data` *A sample DCE-MRI data set.*

Description

A simulated data set based on the extended Tofts model that includes time and AIF vectors, contrast agent concentration-time maps and an ROI mask.

Usage

```
data(dcemri.data)
```

Format

The format is: List of 4

$ vectorTimes: num [1:89] 0.00000 4.83328 9.66656 14.49984 ...

$ mapCC : num [1:25, 1:25, 1:2, 1:89] NA NA NA NA NA NA ...

$ maskROI : int [1:25, 1:25, 1:2] 0 0 0 0 0 0 0 0 0 0 ...

$ vectorAIF : num [1:25] -1.0546669 -15.1168922 13.4470030 ...

Details

A simulated four-slice DCE-MRI data set was generated using the extended Tofts model with mean parameter values set to $K^{trans} = 0.22\ min^{-1}$ and $k_{ep} = 1.1\ min^{-1}$ for all voxels in each slice. Slices 1 and 3 have v_b set to 0 while slices 2 and 4 have v_b set to 0.05. Prior to contrast agent time course simulation for each voxel, the three model parameters (K^{trans}, k_{ep}, v_b) are multiplied by a random variable drawn from a normal distribution with mean=1 and sd=0.2 (slice 1 and 2) or sd=0.3 (slices 3 and 4). An additional level of noise is added to each voxel by multipliying every simulated contrast agent concentration by a random variable drawn from a normal distribution of mean=1 and sd=0.25 (slices 1 and 2) or sd=0.75 (slices 3 and 4).

See Also

`KAT`, `KAT.checkData`, `KAT.plot`

Examples

```
data(dcemri.data, package="KATforDCEMRI")
```

KAT *Kinetic Analysis Tool for DCE-MRI*

Description

Fits the selected model structure to voxel-wise contrast agent concentration data.

Usage

```
KAT(file = "concatenate.KAT.with.KAT.checkData.RData",
results_file="my_results", method.optimization = "L-BFGS-B",
show.rt.fits = FALSE, param.for.avdt = "Ktrans", range.map = 1.5,
cutoff.map = 0.85, export.matlab = TRUE, export.RData = TRUE,
verbose=FALSE, show.errors = FALSE, try.silent=TRUE, fracGTzero = 0.75,
AIF.shift = "", Force.AIF.peak = FALSE, tlag.Tofts.on = FALSE,
est.per.voxel.tlag = FALSE, ...)
```

Arguments

`file`	Specify the file to be analyzed.
`results_file`	Specify the absolute path to the folder, including file name with no extension (.RData and/or .mat will be automatically added) of the file where results are to be saved.
`method.optimization`	Optimization method (`Nelder-Mead`, `BFGS`, `CG`, `L-BFGS-B`, `SANN`); default=`L-BFGS-B`.
`show.rt.fits`	Shows voxel-wise fits as each ROI is processed (default=`FALSE`).
`param.for.avdt`	Select extended Tofts model param to display using avdt (`Ktrans`, `kep`, `ve`, `vb`; default=`Ktrans`).
`range.map`	Specifies range of color scale relative to the max value within map (typically a value between 1 and 3; default=1.5).
`cutoff.map`	Truncate parametric map values by max value $\times$ cutoff (typically a value between 0 and 1; default=0.85).
`export.matlab`	Save results in a matlab file? (default=`TRUE`). NOTE: matlab files are intended only for use with MATLAB and are not meant to be read back into R for viewing with the advanced voxel diagnosis tool.
`export.RData`	Save results in an RData file? (default=`TRUE`).
`verbose`	Should voxel-wise contrast agent curves and other voxel specific information be printed in the terminal during the parameter estimation process? (default=`FALSE`).
`show.errors`	Should errors messages be printed while KAT is running? Default is `show.errors = FALSE`.
`try.silent`	Should the `silent` argument within `try` functions be TRUE or FALSE? Default is `try.silent=TRUE`.

`fracGTzero` Voxels are excluded from analysis if less than 'fracGTzero' of contrast agent concentrations in a voxel time series are greater than zero. (a value between 0 and 1; default is `fracGTzero = 0.75`).

`AIF.shift` Specify if your vascular input function is based on arterial or venous data. Possible values are `"ARTERY"` or `"VEIN"` (or `"NONE"` if you prefer to not estimate the t_{lag} parameter). This argument must be specified when running `KAT`.

`Force.AIF.peak` Do you want to force the peak values of the shifted Vascular input Function to be equal to the peak value of the original, raw VIF that is read into `KAT`? The value of this argument is ignored if `AIF.shift="NONE"`. (default=`FALSE`).

`tlag.Tofts.on` Do you want to estimate t_{lag} for the Tofts model (`tlag.Tofts.on = TRUE`)? If `tlag.Tofts.on = FALSE`, t_{lag} for the Tofts model will be set equal to the t_{lag} value estimated for the extended Tofts model. If `tlag.Tofts.on = TRUE` a single t_{lag} value will be estimated based on the median contrast agent profile over the slice of interest. Use with caution, since there may be parameter identifiability issues associated with estimated t_{lag} when fitting the Tofts model to data. (default=`FALSE`).

`est.per.voxel.tlag` Do you want to estimate t_{lag} on a per-voxel basis for the extended Tofts model (`est.per.voxel.tlag = TRUE`)? Use with caution, since there may be parameter identifiability issues associated with estimated t_{lag} on a per-voxel basis. Note that this argument does not impact per-voxel tlag values within the Tofts model, which will always use t_{lag} values based on median contrast agent profiles. cf. `tlag.Tofts.on`.

`...` Pass arguments to functions within `KAT`.

Details

Demo

Run the KAT benchmark test by typing

```
R> demo(KAT,ask=FALSE)
```

at the R prompt, to analyze the simulated DCE-MRI data set described in `dcemri.data`.

Model equations [refs. 1-2]

Tofts Model

$$\frac{dC_t(t)}{dt} = K^{trans}\text{VIF}(t \pm t_{lag}) - k_{ep}C_t(t)$$

and

$$C(t) = C_t(t).$$

Extended Tofts Model

$$\frac{dC_t(t)}{dt} = K^{trans}\text{VIF}(t \pm t_{lag}) - k_{ep}C_t(t)$$

and

$$C(t) = v_b \text{VIF}(t \pm t_{lag}) + C_t(t),$$

where

$$C_t = \text{tissue/region of interest}$$

and

$$C(t) : \text{measurement model for ROI corresponding to observed CA conc.}$$

VIF$(t \pm t_{lag})$ represents the Vascular Input Function as VIF$(t + t_{lag})$ if the measured VIF is based on arterial data or VIF$(t - t_{lag})$ if the measured VIF is based on venous data.

Objective Function [ref. 3]

The objective function based on maximum likelihood can be written as

$$\text{OF}_M = \frac{1}{n_D} \sum_{i=1}^{n_D} \left[log \left(\frac{1}{\text{SD}_i^2} \right) + \left(\frac{(y_i - s(\hat{p}, t_i))^2}{\text{SD}_i^2} \right) \right],$$

where

$$\text{SD}_i = \text{standard deviation of each data point } i \text{ in the intensity/concentration time curve,}$$

$$y_i = \text{data point } i \text{ in the intensity/concentration time curve,}$$

$$s(\hat{p}, t_i) = \text{simulated data point at parameter vector } \hat{p} \text{ and time point } t_i,$$

and

$$n_D = \text{number of data points in the intensity/concentration time curve.}$$

If observed data is unweighted, i.e., SD$_i = 1$, OF$_M$ is equal to the mean residual sum of squares, OF$_R$, or

$$\text{OF}_R = \frac{\sum_{i=1}^{n_D} (y_i - s(\hat{p}, t_i))^2}{n_D} = \frac{RSS}{n_D} = \overline{RSS}.$$

The objective function implemented in KAT *is written as*

$$\text{OF}_{KAT} = RSS = \sum_{i=1}^{n_D} (y_i - s(\hat{p}, t_i))^2.$$

Model discrimination [ref. 4]

Fits of the Tofts and Extended Tofts model to the intensity/concentration time curve are compared via the Akaike Information Criterion (AIC), written generally as

$$\text{AIC} = -2 \cdot \text{log-likelihood} + n_P.$$

When applying least squares regression, i.e., OF_{KAT}, to observed data with Gaussian variability, the AIC is written as

$$\text{AIC} = n_D \cdot log\left(\text{OF}_R\right) + 2(n_P + 1).$$

A correction term for small sample sizes $(n_D/n_P < 40)$ can be derived, yielding

$$\text{AIC}_c = n_D \cdot log\left(\text{OF}_R\right) + 2(n_P + 1) + \frac{2(n_P + 1)(n_P + 2)}{n_D - n_P - 2},$$

where

$$n_P = \text{number of estimated model parameters.}$$

Coefficients of Variation (CVs) for estimated parameters [refs. 5-6]

The Hessian matrix $\mathbf{H}(\hat{p})$ is calculated numerically by R *during the parameter estimation process, so that the covariance matrix (cov) and %CVs for model parameters estimated using the OF_{KAT}, i.e., RSS, objective function may be* **approximated** *as*

$$cov(\hat{p}) = \frac{n_P \cdot \text{OF}_{KAT}}{n_D - n_P}\mathbf{H}^{-1}(\hat{p})$$

and

$$\%\text{CV}(\hat{p}) = \frac{\sqrt{\text{diag}[cov(\hat{p})]}}{\hat{p}} \times 100\%,$$

where $diag[cov(\hat{p})]$ is a vector composed of the diagonal elements of cov and $\hat{p}$ is the vector of final parameter estimates. Note that this method for calculating %CVs assumes that variability in measured data points follows a Gaussian distribution. Thus, large outlier data points in the concentration/intensity curve, for example those caused by patient motion, may inflate estimated %CVs.

Contents of output file

`args`: List of all arguments specified when running the `KAT` function plus a few additional values generated during the run.

`cc`: `nx` x `ny` x `nt` array of voxel-wise contrast agent concentration/intensity-time curves for all voxels within the Field of View.

`ccroi`: `nx` x `ny` x `nt` array of voxel-wise contrast agent concentration/intensity-time curves for all voxels within the Region of Interest.

`ccmedian`: Median contrast agent-time profile within the Region of Interest.

`maptimes`: `nt` x `1` time vector.

aif: nt x 1 Vascular Input Function.

aifshifted: nt x 1 Time shifted (by t_{lag}) Vascular Input Function.

maskroi: nx x ny array indicating the region of interest.

mapKtransxT: nx x ny array of Ktrans values estimated using the extended Tofts model.

mapKtransxTcv: nx x ny array of %CVs associated with Ktrans values in mapKtransxT.

mapkepxT: nx x ny array of kep values estimated using the extended Tofts model.

mapkepxTcv: nx x ny array of %CVs associated with kep values in mapkepxT.

mapvbxT: nx x ny array of vb values estimated using the extended Tofts model.

mapvbxTcv: nx x ny array of %CVs associated with vb values in mapvbxT.

mapvexT: nx x ny array of ve values estimated using the extended Tofts model. Note that v_e is not directly fitted to the concentration/intensity data but is calculated as $v_e = K^{trans}/k_{ep}$

mapOptimValuexT: nx x ny array of objective function values for voxels where the extended Tofts model has successfully converged (convergence/exit code=0; see ?optim).

mapfitfailuresxT: Map indicating per voxel optimization exit codes for the extended Tofts model. 0: indicates successful completion. 1: indicates that the iteration limit maxit had been reached. 10: indicates degeneracy of the Nelder-Mead simplex. 51: indicates a warning from the L-BFGS-B method; see component message for further details. 52: indicates an error from the L-BFGS-B method; see component message for further details. 99: indicates a try error (optimization routine crashed). -2: indicates that voxel failed fracGTzero test. Voxels with exit codes > 0 will appear white when using the interactive AVDT and are excluded from subsequent analysis.

paramestmedianxT: List of median values of all extended Tofts model parameters fitted on a voxel-wise basis to contrast agent curves within the ROI; includes the percent of total fitted voxels that are classified as fit failures.

roimedianfittedxTofts: Simulated contrast agent-time profile generated by fitting the extended Tofts model to median contrast agent values within the Region of Interest.

paramestwholeroixTofts: Model parameters estimated by fitting the extended Tofts model to median concentration/intensity data across the Region of Interest. These parameters are used to generate roimedianfittedxTofts.

cvwholeroixTofts: %CVs for extended Tofts model parameters listed in paramestwholeroixTofts.

mapKtransT: nx x ny array of Ktrans values estimated using the Tofts model.

mapKtransTcv: nx x ny array of %CVs associated with Ktrans values in mapKtransT.

mapkepT: nx x ny array of kep values estimated using the Tofts model.

mapkepTcv: nx x ny array of %CVs associated with kep values in mapkepT.

mapveT: nx x ny array of ve values estimated using the Tofts model. Note that v_e is not directly fitted to the concentration/intensity data but is calculated as $v_e = K^{trans}/k_{ep}$.

mapOptimValueT: nx x ny array of objective function values for voxels where the Tofts model has successfully converged (convergence/exit code=0; see ?optim).

mapfitfailuresT: Map indicating per voxel optimization exit codes for the Tofts model. 0: indicates successful completion. 1: indicates that the iteration limit maxit had been reached. 10: indicates degeneracy of the Nelder-Mead simplex. 51: indicates a warning from the L-BFGS-B method; see component message for further details. 52: indicates an error from the L-BFGS-B

method; see component message for further details. 99: indicates a try error (optimization routine crashed). -2: indicates that voxel failed `fracGTzero` test. Voxels with exit codes > 0 will appear white when using the interactive AVDT and are excluded from subsequent analysis.

`paramestmedianT`: List of median values of all Tofts model parameters fitted on a voxel-wise basis to contrast agent curves within the ROI; includes the percent of total fitted voxels that are classified as fit failures.

`roimedianfittedTofts`: Simulated contrast agent-time profile generated by fitting the Tofts model to median contrast agent values within the Region of Interest.

`paramestwholeroiTofts`: Model parameters estimated by fitting the Tofts model to median concentration/intensity data across the Region of Interest. These parameters are used to generate `roimedianfittedTofts`.

`proctimetotal`: Total processing time in minutes.

`roiplotparams`: Cropping coordinates applied to the FOV and upper limit of color bar for visualization of parametric maps via the advanced voxel diagnostic tool (AVDT).

`KATversion`: Version of KATforDCEMRI used to generate this output file.

`mapAICxT`: `nx` x `ny` array of AIC_c values for per-voxel fits of the extended Tofts model to concentration/intensity data.

`mapAICT`: `nx` x `ny` array of AIC_c values for per-voxel fits of the Tofts model to concentration/intensity data.

`mapAICcompare`: `nx` x `ny` `nx` x `ny` array that contains a "1" for voxels with a lower (lower=better model) AIC for the extended Tofts model or a "2" for voxels with a lower AIC for the Tofts model.

`nx`: x dimension of the FOV.

`ny`: y dimension of the FOV.

`nt`: number of elements in the time vector (number of time points).

`ccFittedxT`: `nx` x `ny` x `nt` array of extended Tofts model simulations fitted to voxel-wise contrast agent concentration-time data within the ROI.

`ccFittedT`: `nx` x `ny` x `nt` array of Tofts model simulations fitted to voxel-wise contrast agent concentration-time data within the ROI.

`p0T`: Initial parameter values for the Tofts model where $K^{trans}(0)$ and $k_{ep}(0)$ are estimated using the numerical deconvolution method described in the `DATforDCEMRI` package refs **[refs 7-8]**.

`p0xT`: Initial values for the extended Tofts model where $K^{trans}(0)$ and $k_{ep}(0)$ are the same as those used for `p0T`. Initial values for v_b and t_{lag} are set to nominal values (0.05 and 7.2 seconds), when fitting the model to median data. Initial values for v_b and t_{lag}, when fitting the xTofts model to per-voxel data, are set to those values estimated based on fits to the median data.

`IRFresults`: Contains results of noncompartmental analysis of the estimated Impulse Response Function (IRF), where `AUC` is the area under the curve (AUC) of the IRF and is analogous to the Tofts parameter v_e, `AUCMRT` is the AUC of the IRF divided by the Mean Residence Time (MRT) of the IRF and is analogous to the Tofts parameter K^{trans} and `AUCMRT.divby.AUC` is AUCMRT divided by AUC (equal to 1/MRT) and is analogous to the Tofts parameter k_{ep}. Each of these parameters is either corrected for truncation error and contribution of v_b using nominal values (`corrnom`), as described in the entry for `p0xT`, or the actual values estimated based on fitting the extended Tofts model to median intensity/concentration data (`corr`). The method for truncation correction is described in **[ref 7]**.

mapEF: Map indicating enhancing voxel within the specified region of interest, where a "1" indicates enhancement.

Author(s)

Gregory Z. Ferl

References

Model equations

[1] Tofts P, Kermode A (1991) doi: 10.1002/mrm.1910170208

[2] Tofts et al. (1999) https://www.ncbi.nlm.nih.gov/pubmed/10508281

[3] Ferl GZ, Port RE (2012) doi: 10.1038/clpt.2012.63

Objective Function

[4] Barrett PHR, Bell BM, Cobelli C, Golde H, Schumitzky A, Vicini P, and Foster DM (1998) doi: 10.1016/S00260495(98)900646

Model discrimination

[5] Glatting G, Kletting P, Reske SN (2007). doi: 10.1118/1.2794176

Coefficients of Variation (CVs) for estimated parameters

[6] Venables WN, Smith DM, R Core Team (2012) https://CRAN.R-project.org/doc/manuals/R-intro.pdf

R package for numerical deconvolution

[7] Ferl GZ, Xu L, Friesenhahn M, Bernstein LJ, Barboriak DP, Port RE (2010) doi: 10.1002/mrm.22335

[8] Ferl GZ (2011) doi: 10.18637/jss.v044.i03

See Also

KAT.checkData, KAT.plot, dcemri.data

Examples

```
## Create temporary directory for example code output files
temp_dir <- tempdir(check=FALSE)
##
current_dir <- getwd()
setwd(temp_dir)
##
## Run example code
demo(KAT, ask=FALSE)
##
setwd(current_dir)
##
## ANALYZE DATA FROM A SINGLE DCE-MRI SCAN
##
## Load MATLAB files into R
## R> aif <- readMat("mydatafile-AIF.mat")$aif
```

```
## R> ct <- readMat("mydatafile-CT.mat")$ct
## R> roi <- readMat("mydatafile-ROILES.mat")$roi
## R> tvec <- readMat("mydatafile-TVEC.mat")$tvec
##
## Check that the dimensionality of the loaded data is consistent and save
## as a single R object or RData file
## R> dcemri.data <- KAT.checkData(file.name="mydatafile", vector.times=tvec,
##    map.CC=ct, mask.ROI=roi, vector.AIF=aif)
##
## Fit the Tofts and extended Tofts model to all ROIs in RData file
## R> KAT(file="mydatafile.RData", results_file= "mydatafile_out",
## show.rt.fits=TRUE, AIFshift="VEIN")
##
## Plot all ROIs in a single figure
## R> KAT.plot(F1="mydatafile_out_slice3.RData",
##    F2="mydatafile_out_slice4.RData", F3="mydatafile_out_slice5.RData",
##    F4="mydatafile_out_slice6.RData")
##
## Visualize and explore a parametric map for a single ROI
## R> KAT(file="mydatafile_out_slice6.RData")
```

`KAT.checkData` *Checks and converts your data to the RData file format.*

Description

Load your data into an R session and save as an RData file that can be analyzed by the KAT function. Also check that dimensions of vectors and arrays are consistent.

Usage

```
KAT.checkData(file.name, vector.times, map.CC, mask.ROI, vector.AIF, map.tlag=NULL,
write.data.to.file=TRUE)
```

Arguments

`file.name`	Give a name to the RData file that will be generated with this function. A `.RData` extension will automatically be added.
`vector.times`	The nt x 1 time vector; can have units of seconds or minutes. KAT will automatically assign units based on the following assumptions: units are minutes if $t_{max} < 100$ and seconds if $t_{max} \geq 100$. Please make sure that these assumptions are consistent with your data. You will have to manually convert the time vector into seconds or minutes prior to running `KAT.checkData` if the time vector specified by `vector.times` has other units.
`map.CC`	The nx x ny x ns x nt contrast agent intensity/concentration array.
`mask.ROI`	The nx x ny x ns ROI mask array where voxels within the ROI are assigned a 1 and those outside assigned a 0.
`vector.AIF`	The nt x 1 arterial (vascular) input function.

`map.tlag` The nx x ny x ns array that contains per-voxel tag times estimated outside of KAT, to be applied to the vascular input function. Units must be same as those used for vector.times. This argument is optional.

`write.data.to.file`
Should the original data, loaded into R, be saved in a single RData file for future use? Default=TRUE.

NOTE: if set to FALSE, usage for this function must be exactly as follows:

R> dcemri.data <- KAT.checkData(args)

R> KAT(args)

where the `file` argument is **not** specified when calling KAT().

Value

Returns an RData file that can be read by the `KAT` function.

Note

The `KAT` function can also read data stored as an uncompressed MATLAB 5 file.

Author(s)

Gregory Z. Ferl

See Also

`KAT`, `KAT.plot`, `dcemri.data`

Examples

```
## Create temporary directory for benchmark example code output files
temp_dir <- tempdir(check=FALSE)
##
current_dir <- getwd()
setwd(temp_dir)
##
## Run example code
data(dcemri.data, package="KATforDCEMRI")
a1=dcemri.data$vectorTimes
a2=dcemri.data$mapCC
a3=dcemri.data$maskROI
a4=dcemri.data$vectorAIF
KAT.checkData("f",vector.times=a1,map.CC=a2,mask.ROI=a3,vector.AIF=a4,write.data.to.file=TRUE)
##
setwd(current_dir)
```

KAT.plot *Plots multiple image slices.*

Description

Plots multiple image slices on the same color scale within a single PDF file.

Usage

```
KAT.plot(F1=0, F2=0, F3=0, F4=0, F5=0, F6=0, F7=0,
F8=0, plot.param="Ktrans", range.map = 1.5, cutoff.map=0.85, ...)
```

Arguments

F1	KAT output file containing parametric map 1.
F2	KAT output file containing parametric map 2.
F3	KAT output file containing parametric map 3.
F4	KAT output file containing parametric map 4.
F5	KAT output file containing parametric map 5.
F6	KAT output file containing parametric map 6.
F7	KAT output file containing parametric map 7.
F8	KAT output file containing parametric map 8.
plot.param	Which parameter will be plotted? Can be set to Ktrans, kep, vb or ve. (Default=Ktrans).
...	Arguments passed on to inner functions.
range.map	Specifies range of color scale relative to the max value within map (typically a value between 1 and 3; default=1.5).
cutoff.map	Truncate parametric map values by max value x cutoff (typically a value between 0 and 1; default=0.85).

Details

For n slices, 3 x n figure panels will be generated where n is the number of slices to be plotted. MAP is the parametric map for the slice of interest, while AIC is the model discrimination map for the slice of interest. ROI is the median contrast agent concentration-time profile over all voxels within the region of interest shown with associated estimated extended Tofts model parameters.

slice 1—-slice 2—-slice 3—-slice 4—-slice 5—-slice 6—-slice 7—-slice 8

[MAP]—[MAP]—[MAP]—[MAP]—[MAP]—[MAP]—[MAP]—[MAP]

[AIC]—-[AIC]—-[AIC]—-[AIC]——[AIC]—-[AIC]—-[AIC]—-[AIC]

[ROI]—-[ROI]—-[ROI]—-[ROI]—-[ROI]—-[ROI]—-[ROI]—-[ROI]

Author(s)

Gregory Z. Ferl

Examples

```
## Create temporary directory for example code output files
temp_dir <- tempdir(check=FALSE)
##
current_dir <- getwd()
setwd(temp_dir)
##
## Run example code
demo(KAT, ask=FALSE)
file1="KAT_benchmark_test-full_slice1.RData"
file2="KAT_benchmark_test-full_slice2.RData"
file3="KAT_benchmark_test-full_slice3.RData"
file4="KAT_benchmark_test-full_slice4.RData"
KAT.plot(F1=file1, F2=file2, F3=file3, F4=file4, export.matlab=FALSE)
##
setwd(current_dir)
```

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