

# Package ‘EZFragility’

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**Title** Compute Neural Fragility for Ictal iEEG Time Series

**Version** 2.1.1

**Description** Provides tools to compute the neural fragility matrix from intracranial electrocorticographic (iEEG) recordings, enabling the analysis of brain dynamics during seizures. The package implements the method described by Li et al. (2017) <doi:10.23919/ACC.2017.7963378> and includes functions for data preprocessing ('Epoch'), fragility computation ('calcAdjFrag'), and visualization.

**License** GPL (>= 3)

**Encoding** UTF-8

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**Depends** R (>= 4.1.0), Epoch

**LazyData** true

**Imports** stats, methods, ggplot2 (>= 3.4.0), viridis, ggtext, glue, rlang, foreach, progress, ramify, reshape2

**Suggests** knitr, rmarkdown, testthat (>= 3.0.0), doSNOW, gsignal

**Config/testthat/edition** 3

**VignetteBuilder** knitr

**URL** <https://github.com/Jiefei-Wang/EZFragility>

**NeedsCompilation** no

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|             |                                                                              |
|-------------|------------------------------------------------------------------------------|
| calcAdjFrag | <i>Calculate adjacency matrices and fragility matrix from iEEG recording</i> |
|-------------|------------------------------------------------------------------------------|

---

**Description**

The function calculates the neural fragility column from an adjacency matrix in each time window

**Usage**

```
calcAdjFrag(  
  epoch,  
  window,  
  step,  
  lambda = NULL,  
  nSearch = 100L,  
  progress = FALSE,  
  parallel = FALSE  
)
```

**Arguments**

|          |                                                                                                                                                                                                                                           |
|----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| epoch    | Matrix or Epoch object. iEEG data matrix or Epoch object. If matrix, the row names are the electrode names and the column names are the time points. For a matrix input, the sampling rate is assumed to be 1 Hz and the start time is 0. |
| window   | Integer. The number of time points to use in each window                                                                                                                                                                                  |
| step     | Integer. The number of time points to move the window each time                                                                                                                                                                           |
| lambda   | Numeric. The lambda value for regularization to use in the ridge regression. If NULL, the lambda will be chosen automatically ensuring that the adjacent matrix is stable (see details)                                                   |
| nSearch  | Integer. Number of instable eigenvalues with norm=1 to search for the minimum norm perturbation. This parameter is used only when the lambda is NULL                                                                                      |
| progress | Logical. If TRUE, print progress information. If parallel is TRUE, this option only support the doSNOW backend.                                                                                                                           |
| parallel | Logical. If TRUE, use parallel computing. Users must register a parallel backend with the foreach package                                                                                                                                 |

**Details**

1/ For each time window  $i$ , a discrete stable Linear time system (adjacency matrix) is computed named  $A_i$  such that  $A_i x(t) = x(t + 1)$ . The 'lambda' option is the regularization parameter for the ridge regression. lambda=NULL(default) will find a lambda value that ensures the stability of the estimated  $A_i$ .

2/For each stable estimated  $A_i$ , the minimum norm perturbation  $\Gamma_{ik}$  (k index of the electrodes) for column perturbation is computed. Each column is normalized  $\frac{\max(\Gamma_i) - \Gamma_{ik}}{\max(\Gamma_i)}$

**Value**

A Fragility object

**Source**

Recreation of the method described in Li A, Huynh C, Fitzgerald Z, Cajigas I, Brusko D, Jagid J, et al. Neural fragility as an EEG marker of the seizure onset zone. Nat Neurosci. 2021 Oct;24(10):1465–74 ([pubmed](#)). We have found solutions to fill up missing details in the paper method description

**Examples**

```
## A dummy example with 5 electrodes and 20 time points
data <- matrix(rnorm(100), nrow = 5)
## create an Epoch object
epoch <- Epoch(data, startTime = 0, samplingRate = 1)
windowNum <- 10
step <- 5
lambda <- 0.1
calcAdjFrag(
  epoch = epoch, window = windowNum,
```

```

    step = step, lambda = lambda, progress = TRUE
  )

## A more realistic example with parallel computing

if (requireNamespace("doSNOW")) {
  ## Register a SNOW backend with 4 workers
  library(parallel)
  library(doSNOW)
  cl <- makeCluster(4, type = "SOCK")
  registerDoSNOW(cl)

  data("pt01EcoG")
  window <- 250
  step <- 125
  title <- "PT01 seizure 1"
  calcAdjFrag(
    epoch = pt01EcoG, window = window,
    step = step, parallel = TRUE, progress = TRUE
  )

  ## stop the parallel backend
  stopCluster(cl)
}

```

---

checkIndex

*Check and keep valid index only*


---

### Description

Check and keep valid index only

### Usage

```
checkIndex(indices, names)
```

### Arguments

|         |                                                   |
|---------|---------------------------------------------------|
| indices | Numeric or character index to check               |
| names   | Character. All names corresponding to the indices |

---

|             |                                |
|-------------|--------------------------------|
| estimateSOZ | <i>Find Seizure Onset Zone</i> |
|-------------|--------------------------------|

---

### Description

The function estimates the seizure onset zone (SOZ). For each row, it calculates the maximum, minimum, or mean of row. The rows with the highest values are considered as the SOZ.

### Usage

```
estimateSOZ(
  x,
  method = c("mean", "median", "max", "min"),
  proportion = 0.1,
  ...
)
```

### Arguments

|            |                                                                                                                                   |
|------------|-----------------------------------------------------------------------------------------------------------------------------------|
| x          | Fragility object                                                                                                                  |
| method     | Character. The method to use to find the onset zone. Must be one of 'max', 'min', or "mean"                                       |
| proportion | Numeric. The proportion of electrodes to consider as the onset zone. The electrode number will be rounded to the nearest integer. |
| ...        | Additional arguments                                                                                                              |

### Value

A vector of electrode names, or indices if the electrode names are NULL

---

|              |                                                                    |
|--------------|--------------------------------------------------------------------|
| fragilityRow | <i>Compute the normalized fragility row for adjacency matrix A</i> |
|--------------|--------------------------------------------------------------------|

---

### Description

The matrix A is used for the regression:  $A * x(t) = x(t+1)$

### Usage

```
fragilityRow(A, nSearch = 100, normalize = TRUE)
```

### Arguments

|           |                                                                      |
|-----------|----------------------------------------------------------------------|
| A         | Numeric. Adjacency Matrix                                            |
| nSearch   | Integer. Number of eigenvalues tried to find the minimum norm vector |
| normalize | Logical. If TRUE, the fragility row is normalized                    |

---

|          |                                                                                 |
|----------|---------------------------------------------------------------------------------|
| fragStat | <i>Compute quantiles, mean and standard deviation for two electrodes groups</i> |
|----------|---------------------------------------------------------------------------------|

---

### Description

Compute quantiles, mean and standard deviation for two electrodes groups

### Usage

```
fragStat(frag, groupIndex = NULL, groupName = "SOZ", ranked = FALSE)
```

### Arguments

|            |                                                                         |
|------------|-------------------------------------------------------------------------|
| frag       | A Fragility object from calcAdjFrag                                     |
| groupIndex | Integer or string. A group of electrodes to mark                        |
| groupName  | Character. Name of the group of electrodes, default is "SOZ"            |
| ranked     | Logical. If TRUE, use the ranked fragility matrix from Fragility object |

### Value

list of 5 items with quantile matrix, mean and sdv from both electrodes groups

### Examples

```
data("pt01Frag")
data("pt01EcoG")
## sozNames is the name of the electrodes we assume are in the SOZ
sozNames <- metaData(pt01EcoG)$sozNames
pt01fragstat <- fragStat(frag = pt01Frag, groupIndex = sozNames)
```

---

|                       |                                                                |
|-----------------------|----------------------------------------------------------------|
| nrow,Fragility-method | <i>Get the number of rows or columns of a Fragility object</i> |
|-----------------------|----------------------------------------------------------------|

---

### Description

Get the number of rows or columns of a Fragility object

### Usage

```
## S4 method for signature 'Fragility'
nrow(x)

## S4 method for signature 'Fragility'
ncol(x)
```

**Arguments**

x                      A Fragility object

**Value**

- `nrow(x)`: The number of rows (electrodes) in the fragility matrix.
- `ncol(x)`: The number of columns (time points) in the fragility matrix.
- `dim(x)`: A vector of length 2 containing the number of rows and columns in the fragility matrix.

---

plot,Fragility,missing-method

*Visualization functions (raw signal, fragility matrix)*

---

**Description**

`plot`: plot fragility heatmaps with electrodes marked as soz colored

`plotFragQuantile`: Plot Fragility time quantiles for two electrodes groups

`plotFragQuantile`: Plot Fragility time distribution for two electrodes groups

**Usage**

```
## S4 method for signature 'Fragility,missing'
```

```
plot(
  x,
  y,
  groupIndex = NULL,
  maxLabels = 50,
  ranked = FALSE,
  x.lab.size = 10,
  y.lab.size = 10
)
```

```
plotFragQuantile(
  frag,
  groupIndex = NULL,
  groupName = "SOZ",
  x.lab.size = 10,
  y.lab.size = 10
)
```

```
plotFragDistribution(
  frag,
  groupIndex = NULL,
  groupName = "SOZ",
```

```

bandType = c("SEM", "SD"),
rollingWindow = 1,
ranked = FALSE,
x.lab.size = 10,
y.lab.size = 10
)

```

## Arguments

|                            |                                                                                                                                                               |
|----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>x</code>             | Fragility object from <code>calcAdjFrag</code>                                                                                                                |
| <code>y</code>             | Not used (for S4 method compatibility)                                                                                                                        |
| <code>groupIndex</code>    | Integer or string. A group of electrodes to mark                                                                                                              |
| <code>maxLabels</code>     | Integer. Maximum number of labels to show on y-axis. Default is 50. The actual number of labels may be less than this value if there are too many electrodes. |
| <code>ranked</code>        | Logical. If TRUE, use the ranked fragility matrix from Fragility object                                                                                       |
| <code>x.lab.size</code>    | Numeric. Size of x-axis labels. Default is 4.                                                                                                                 |
| <code>y.lab.size</code>    | Numeric. Size of y-axis labels. Default is 10                                                                                                                 |
| <code>frag</code>          | Fragility object from <code>calcAdjFrag</code>                                                                                                                |
| <code>groupName</code>     | Character. Name of the group of electrodes, default is "SOZ"                                                                                                  |
| <code>bandType</code>      | Character. The type of band to use, either "SEM" or "SD". Default is "SEM".                                                                                   |
| <code>rollingWindow</code> | Integer. Window size for rolling average smoothing. Default is 1 (no smoothing).                                                                              |

## Value

A ggplot object

## Examples

```

data("pt01EcoG")

## sozNames is the name of the electrodes we assume are in the SOZ
sozNames <- metaData(pt01EcoG)$sozNames

## precomputed fragility object
data("pt01Frag")

## plot the fragility heatmap
plot(pt01Frag, groupIndex = sozNames)

## plot the fragility quantiles
plotFragQuantile(frag = pt01Frag, groupIndex = sozNames)

## plot the fragility distribution
plotFragDistribution(frag = pt01Frag, groupIndex = sozNames)

## plot with smoothing
plotFragDistribution(frag = pt01Frag, groupIndex = sozNames, rollingWindow = 2)

```



pt01EcoG

*Pt01 seizure 1 around seizure onset***Description**

This data corresponds to the first seizure of patient from the Fragility Data Set. EcoG recording gathered in collaboration with the National Institute of Health. The data contains only the good channels. It has been notch filtered and common average referenced in RAVE. The time range for full data is (-10:10s). Due to the size limit of the package, The full data has been epoched -1:2s around the seizure onset. The acquisition frequency is 1000 Hz

**Usage**

```
## EEG data
data(pt01EcoG)
```

**Format**

pt01EcoG: A Matrix with 84 rows (electrodes) and 3000 columns (time points)

pt01Frag: A fragility object results of applying the main function calcAdjFrag to pt01EcoG with window = 250 and step = 125

**Source**

Fragility Multi-Center Retrospective Study ([OpenNeuro](#))

ridge

*fit a generalized linear model to compute adjacency matrix A***Description**

A  $x(t) = x(t+1)$

**Usage**

```
ridge(xt, xtp1, lambda)
```

**Arguments**

|        |                                                                                                              |
|--------|--------------------------------------------------------------------------------------------------------------|
| xt     | matrix. iEEG time series for a given window, with electrodes names as rows and time points as columns        |
| xtp1   | matrix. the iEEG time serie at the next time point, with electrodes names as rows and time points as columns |
| lambda | Numeric Vector. A user supplied lambda sequence.                                                             |

**Value**

adjacency matrix A

---

|         |                    |
|---------|--------------------|
| ridgeR2 | <i>computes R2</i> |
|---------|--------------------|

---

**Description**

computes R2

**Usage**

ridgeR2(xt, xtp1, A)

**Arguments**

- xt                    matrix. iEEG time series for a given window, with electrodes names as rows and time points as columns
- xtp1                matrix. the iEEG time serie at the next time point, with electrodes names as rows and time points as columns
- A                    adjacency matrix

---

|             |                                                |
|-------------|------------------------------------------------|
| ridgeSearch | <i>Ridge Regression for Electrode Readings</i> |
|-------------|------------------------------------------------|

---

**Description**

Ridge regression to compute matrix adjancency matrix A such as  $A \cdot xt = xtp1$  the lambda parmeter is found by dichotomy such that A is stable (all eigenvalues have a norm less than one)

**Usage**

ridgeSearch(xt, xtp1, lambda = NULL)

**Arguments**

- xt                    matrix. iEEG time series for a given window, with electrodes names as rows and time points as columns
- xtp1                matrix. the iEEG time serie at the next time point, with electrodes names as rows and time points as columns
- lambda              Numeric Vector. A user supplied lambda sequence.

**Value**

adjacency matrix A<sub>fin</sub> with lambda as attribute

---

show,Fragility-method    *Print the Fragility object*

---

**Description**

Print the Fragility object

**Usage**

```
## S4 method for signature 'Fragility'
show(object)
```

**Arguments**

object                    A Fragility object

**Value**

the object itself

---

show,FragStat-method    *Print the FragStat object*

---

**Description**

Print the FragStat object

**Usage**

```
## S4 method for signature 'FragStat'
show(object)
```

**Arguments**

object                    A FragStat object

**Value**

the object itself

---

|                    |                                  |
|--------------------|----------------------------------|
| [,Fragility-method | <i>Subset a Fragility object</i> |
|--------------------|----------------------------------|

---

**Description**

Subset a Fragility object

**Usage**

```
## S4 method for signature 'Fragility'
x[i, j, ..., drop = FALSE]
```

**Arguments**

|      |                                                                            |
|------|----------------------------------------------------------------------------|
| x    | A Fragility object                                                         |
| i    | A logical vector or a numeric vector of indices to subset the electrodes   |
| j    | A logical vector or a numeric vector of indices to subset the time windows |
| ...  | Additional arguments (not used)                                            |
| drop | Additional arguments (not used)                                            |

**Value**

A new Fragility object with the subsetting data

---

|                    |                                          |
|--------------------|------------------------------------------|
| \$,FragStat-method | <i>Getters and Setters for S4 object</i> |
|--------------------|------------------------------------------|

---

**Description**

Getters and Setters for S4 object

**Usage**

```
## S4 method for signature 'FragStat'
x$name

## S4 replacement method for signature 'FragStat'
x$name <- value

## S4 method for signature 'Fragility'
x$name

## S4 replacement method for signature 'Fragility'
x$name <- value
```

**Arguments**

|       |              |
|-------|--------------|
| x     | S4 object    |
| name  | Slot name    |
| value | Value to set |

**Value**

S4 object itself or slot value

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