Package: MariNET (via r-universe)

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Title Build Networks from EHRs and Omics Data Using Linear Mixed Models

Version 2.0.0

Description Analyzing longitudinal clinical data from Electronic Health Records (EHRs) using linear mixed models (LMM) and visualizing the results as networks. It includes functions for fitting LMM, normalizing adjacency matrices, and comparing networks. It also allows the integration of omics data (e.g. gene expression or protein abundance) with longitudinal clinical variables, building networks of molecular feature-clinical relationships. The package is designed for researchers in clinical and biomedical fields who need to model longitudinal data and explore relationships between variables. For more details see Bates et al. (2015) <doi:10.18637/jss.v067.i01>.

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`differentiation` *Subtract Two Adjacency Matrices*

Description

This function returns difference matrix between two networks. It is useful for comparing two networks represented by adjacency matrices.

Usage

```
differentiation(matrix1, matrix2)
```

Arguments

`matrix1`	The first adjacency matrix.
`matrix2`	The second adjacency matrix.

Value

a normalized matrix containing values between 0 and 1.

`example_data` *Example Dataset: Psychological and Behavioral Responses*

Description

This dataset contains self-reported psychological and behavioral responses from individuals.

Usage

```
example_data
```

Format

A data frame with multiple rows and 17 variables:

id Unique participant identifier (integer).

Relax Self-reported relaxation level (integer scale).

Irritable Self-reported irritability level (integer scale).

Worry Level of worry experienced (integer scale).

Nervous Self-reported nervousness (integer scale).

Future Concerns about the future (integer scale).

Anhedonia Self-reported lack of enjoyment (integer scale).

Tired Level of tiredness (integer scale).

Hungry Self-reported hunger level (integer scale).

Alone Feeling of loneliness (integer scale).

Angry Level of anger experienced (integer scale).

Social_offline Offline social interactions (integer scale).

Social_online Online social interactions (integer scale).

Music Time spent listening to music (integer scale).

Procrastinate Self-reported procrastination (integer scale).

Outdoors Time spent outdoors (integer scale).

C19_occupied Engagement in activities during COVID-19 (integer scale).

C19_worry Level of worry related to COVID-19 (integer scale).

Home Time spent at home (integer scale).

day Day number of the study (integer).

beep Moment within the day when data was collected (integer).

conc Self-reported concentration level (integer scale).

Details

This dataset was collected from a study examining psychological and behavioral responses to various daily experiences. Each row represents a unique moment of self-reporting.

Source

Reproducible figure for Nature Methods primer paper, Borsboom et al. 2021. This examples contains a *subset* of variables collected and modeled in our covid19 paper. This paper, with full data is available on https://journals.sagepub.com/doi/10.1177/21677026211017839. Eiko Fried, March 14 2021

Examples

```
data(example_data)
head(example_data)
```

`example_omics` *Example Dataset: Simulated Longitudinal Clinical and Omics Data*

Description

This dataset contains fully simulated longitudinal clinical measurements and molecular features (e.g. gene expression) for 80 participants with up to 4 visits. It is intended to illustrate the integration of molecular features with clinical variables using `lmm_integration_analysis()`.

Usage

```
example_omics
```

Format

A data frame with 296 rows and 18 variables:

participant_id Unique participant identifier (character).

visit_month Month of the visit since baseline (0, 12, 24 or 36).

sex Sex of the participant (Female or Male).

age Age of the participant at baseline (years).

Systolic_BP Systolic blood pressure (mmHg).

Diastolic_BP Diastolic blood pressure (mmHg).

Heart_rate Resting heart rate (beats per minute).

BMI Body mass index (kg/m2).

Glucose Fasting blood glucose (mg/dL).

Cholesterol Total blood cholesterol (mg/dL).

GENE1, GENE2, GENE3, GENE4, GENE5, GENE6, GENE7, GENE8 Simulated molecular features (e.g. normalized gene expression).

Details

Data are fully synthetic and do not correspond to any real participant or study. Some molecular features were simulated to be associated with clinical variables: GENE1 with Systolic_BP (positive), GENE2 with Cholesterol (negative), GENE3 with Glucose (positive) and GENE4 with Heart_rate (negative). GENE5 to GENE8 have no association with clinical variables. Around 10% of follow-up visits were removed to mimic missed visits.

Source

Simulated data. The code used to generate the dataset is available in the `data-raw` folder of the package source.

Examples

```
data(example_omics)
head(example_omics)
```

---

lmm_analysis *Perform Longitudinal Analysis with Linear Mixed Models (LMM)*

Description

This function automates the analysis of longitudinal clinical data using linear mixed models. It models clinical variables and returns a weighted matrix of model coefficient scores.

Usage

```
lmm_analysis(
  clinical_data,
  variables_to_scale,
  random_effects = "(1 | participant_id)"
)
```

Arguments

`clinical_data`	Dataframe containing clinical and metadata for participants, including identifier as `participant_id`.
`variables_to_scale`	Character vector of variable names to be analyzed.
`random_effects`	A character string specifying the random effects formula (default: "(1 | participant_id)").

Value

A matrix of model coefficient scores, where rows represent dependent variables and columns represent independent variables.

`lmm_integration_analysis` *Multi-omics Longitudinal Analysis with Linear Mixed Models (LMM)*

Description

This function builds a network between molecular features (e.g. genes or proteins) and clinical variables from longitudinal data using linear mixed models. Two sets of models are fitted: each clinical variable is modeled on all other clinical variables and the molecular features, and each molecular feature is modeled on the clinical variables. The weight of a feature-clinical edge is the mean of both t-values. Clinical-clinical and feature-feature edges are set to zero, so the network only contains feature-clinical edges.

Usage

```
lmm_integration_analysis(
  clinical_data,
  variables_to_scale,
  molecular_features,
  random_effects = "(1 | participant_id)"
)
```

Arguments

`clinical_data`	Dataframe containing clinical data, metadata and molecular features (one column per feature, samples merged with clinical data), including identifier as 'participant_id'.
`variables_to_scale`	Character vector of clinical variable names to be analyzed.
`molecular_features`	Character vector of molecular feature names (columns of 'clinical_data'). Names that are not syntactically valid in R (e.g. "H1-0") are allowed.
`random_effects`	A character string specifying the random effects formula (default: "(1 | participant_id)").

Value

A symmetric matrix of model coefficient scores with clinical variables followed by molecular features.

Examples

```
data(example_omics)
clinical_vars <- c("Systolic_BP", "Diastolic_BP", "Heart_rate", "BMI", "Glucose", "Cholesterol")
molecular_features <- paste0("GENE", 1:8)
net <- lmm_integration_analysis(example_omics, clinical_vars, molecular_features,
                                random_effects = "(1|participant_id)")
round(net[clinical_vars, molecular_features], 2)
```

normalization *Normalization of weighted linear mixed model network matrix.*

Description

This function normalizes weighted adjacency matrix derived from lmm.

Usage

```
normalization(matrix)
```

Arguments

matrix	The adjacency matrix (to be normalized).

Value

a normalized matrix containing values between 0 and 1.

score_matrix *Compute Score Matrix*

Description

This function adjusts an original matrix by copying the lower triangular part from a shifted matrix.

Usage

```
score_matrix(original_matrix, shifted_matrix)
```

Arguments

original_matrix	A numeric matrix representing the original data.
shifted_matrix	A numeric matrix that has been transformed using `shift_matrix()`.

Value

A new matrix with adjusted values in the lower triangular part.

`shift_matrix` *Shifted Matrix Transformation*

Description

This function modifies the shape of a model weights matrix by shifting its elements.

Usage

```
shift_matrix(mat)
```

Arguments

`mat`	A numeric matrix to be transformed.

Value

A shifted version of the input matrix.

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