Package: RhyME (via r-universe)

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Title Beta Regression Cosinor Models for Circadian Methylation Analysis

Version 0.99.3

Description Fits beta cosinor models to methylation measurements using penalized quasi-likelihood (PQL), an optional subject random intercept, adjustment covariates, and an optional empirical Bayes (EB) prior on log precision. Tests rhythmicity with a null-model score test and estimates rhythm parameters from a separate full-model fit.

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URL https://github.com/njuelsdke/RhyME

BugReports https://github.com/njuelsdke/RhyME/issues

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`fitCosinor` *Fit Cosinor Models Across CpG Sites*

Description

Fits beta cosinor models using PQL, with optional random intercepts, adjustment covariates, and an empirical Bayes (EB) prior on log precision. A null-model score test assesses rhythmicity; a full model estimates rhythm parameters.

Usage

```
fitCosinor(
  se,
  time_col = "time",
  subject_col = NULL,
  assay_name = NULL,
  period = 24,
  prior = c("auto", "none"),
  BPPARAM = BiocParallel::bpparam(),
  verbose = TRUE,
  covariates = NULL
)
```

Arguments

`se`	A `SummarizedExperiment` with CpGs in rows and samples in columns. The assay contains numeric beta values in $[0, 1]$, with missing values allowed.
`time_col`	Name of the collection-time column in `colData(se)`, in hours.
`subject_col`	Name of the subject column for a random-intercept model, or `NULL` for a fixed-effects model of independent samples.
`assay_name`	Assay name, or `NULL` to use the first assay.
`period`	Oscillation period in hours. Default is 24.
`prior`	`"auto"` estimates an EB prior; `"none"` uses no prior. A named list with `mean` and positive `sd` supplies a normal prior on log precision. EB estimation requires at least 1,000 usable pilot fits.
`BPPARAM`	A `BiocParallelParam` object. Defaults to `BiocParallel::bpparam()`, which uses the user's registered default backend.
`verbose`	Whether to print fitting progress.
`covariates`	Names of numeric or categorical `colData(se)` columns for adjustment. Covariate coefficients are not returned.

Value

The input `SummarizedExperiment` with these `rowData(se)` columns:

- `RhyME_b0`, `RhyME_b_sin`, `RhyME_b_cos`: logit-scale intercept and sine/cosine coefficients.
- `RhyME_log_phi`, `RhyME_tau`: log precision and random-intercept SD.
- `RhyME_score_chisq`, `RhyME_pvalue`, `RhyME_padj`: score statistic, p-value, and BH-adjusted p-value across all input CpGs.
- `RhyME_logit_amplitude`, `RhyME_amplitude`: logit-scale amplitude and half the marginal mean curve's peak-to-trough difference on the methylation scale.
- `RhyME_phase`, `RhyME_mesor`: peak time in hours in $[0, \text{period})$ and the marginal mean curve averaged over one period.
- `RhyME_converged`: whether both null and full fits converged.

Unusable null fits have `NA` p-values; unusable full fits have `NA` parameter estimates. Usable results from either fit are retained. Phase is undefined at zero amplitude. Existing row annotations are retained; refitting replaces only the result columns listed above. Unprefixed columns from earlier versions are retained as annotations. `metadata(se)$RhyME` stores `design`, `ebPrior`, and `fitSummary`.

See Also

`plotCosinorFit()`

Examples

```
# Independent samples: default fixed-effects model and automatic EB prior.
set.seed(123)
n_cpg <- 1200
time <- rep(seq(0, 20, by = 4), 8)
amplitude <- c(rep(0.6, 240), rep(0, 960))
mu <- plogis(outer(amplitude, sin(2 * pi * time / 24)))
beta <- matrix(rbeta(length(mu), mu * 40, (1 - mu) * 40),
    nrow = n_cpg, dimnames = list(paste0("cg", seq_len(n_cpg)),
        paste0("sample", seq_along(time))))
se_independent <- SummarizedExperiment::SummarizedExperiment(
    assays = list(beta = beta), colData = S4Vectors::DataFrame(time = time))
fit_fixed <- fitCosinor(se_independent,
    BPPARAM = BiocParallel::SerialParam(), verbose = FALSE)
S4Vectors::metadata(fit_fixed)$RhyME$ebPrior

# Repeated measurements: disable EB for this small subset.
ex <- readRDS(system.file("extdata", "example_data.rds", package = "RhyME"))
fit <- fitCosinor(ex$se[seq_len(5), ], subject_col = "subject",
    prior = "none", verbose = FALSE)
head(SummarizedExperiment::rowData(fit), 3)
```

`plotCosinorFit` *Plot Fitted Cosinor Curves*

Description

Plots observed beta values and fitted marginal mean curves over the observed time range, using the design saved by `fitCosinor()`. Curves describe the mean covariate profile; points are not covariate-adjusted.

Usage

```
plotCosinorFit(se, cpgs = NULL, ncol = 3)
```

Arguments

`se`	A `SummarizedExperiment` returned by `fitCosinor()`, with `RhyME_`-prefixed result columns. Refit objects from earlier versions that have only unprefixed results.
`cpgs`	CpG identifiers in panel order. `NULL` selects up to six CpGs with usable estimates, ordered by p-value.
`ncol`	Number of panels per row.

Value

A `ggplot2` object.

See Also

`fitCosinor()`

Examples

```
ex <- readRDS(system.file("extdata", "example_data.rds", package = "RhyME"))
fit <- fitCosinor(ex$se[1, ], subject_col = "subject", prior = "none",
    verbose = FALSE)
plotCosinorFit(fit)
```

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