

Package ‘SpectralTAD’

May 17, 2024

Title SpectralTAD: Hierarchical TAD detection using spectral clustering

Version 1.20.0

Description SpectralTAD is an R package designed to identify Topologically Associated Domains (TADs) from Hi-C contact matrices. It uses a modified version of spectral clustering that uses a sliding window to quickly detect TADs. The function works on a range of different formats of contact matrices and returns a bed file of TAD coordinates. The method does not require users to adjust any parameters to work and gives them control over the number of hierarchical levels to be returned.

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Encoding UTF-8

RoxygenNote 7.2.3

Imports dplyr, PRIMME, cluster, Matrix, parallel, BiocParallel, magrittr, HiCcompare, GenomicRanges, utils

Suggests BiocCheck, BiocManager, BiocStyle, knitr, rmarkdown, microbenchmark, testthat, covr

Depends R (>= 3.6)

VignetteBuilder knitr

biocViews Software, HiC, Sequencing, FeatureExtraction, Clustering

BugReports <https://github.com/dozmorovlab/SpectralTAD/issues>

URL <https://github.com/dozmorovlab/SpectralTAD>

git_url <https://git.bioconductor.org/packages/SpectralTAD>

git_branch RELEASE_3_19

git_last_commit a132d8c

git_last_commit_date 2024-04-30

Repository Bioconductor 3.19

Date/Publication 2024-05-16

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| | |
|------------------|---|
| rao_chr20_25_rep | <i>Contact matrix from Rao 2014, chromosome 20, 25kb resolution</i> |
|------------------|---|

Description

A sparse 3-column contact matrix

Usage

data(rao_chr20_25_rep)

Format

A data.frame with 3 columns and 2125980 rows:

- V1** The genomic loci corresponding to a given row of the contact matrix
- V2** The genomic loci corresponding to a given column of the contact matrix
- V3** Number of contacts between Loci1 and Loci2

Value

A data.frame

Source

Data from Rao SS, Huntley MH, Durand NC, Stamenova EK et al. A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping. Cell 2014 Dec 18;159(7):1665-80. PMID: 25497547. Available at <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE63525>

SpectralTAD

*Hierarchical Spectral Clustering of TADs***Description**

Hierarchical Spectral Clustering of TADs

Usage

```

SpectralTAD(
  cont_mat,
  chr,
  levels = 1,
  qual_filter = FALSE,
  z_clust = FALSE,
  eigenvalues = 2,
  min_size = 5,
  window_size = 25,
  resolution = "auto",
  gap_threshold = 1,
  grange = FALSE,
  out_format = "none",
  out_path = chr
)

```

Arguments

| | |
|-------------|--|
| cont_mat | Contact matrix in either sparse 3 column, n x n or n x (n+3) form where the first three columns are coordinates in BED format. If an x n matrix is used, the column names must correspond to the start point of the corresponding bin. If large mode is selected, then this matrix must be a tab-separated n x n or n x (n+3) and it should be the path to a contact matrix. Required. |
| chr | The chromosome of the contact matrix being analyzed. Required. |
| levels | The number of levels of the TAD hierarchy to be calculated. The default setting is 1. |
| qual_filter | Option to turn on quality filtering which removes TADs with negative silhouette scores (poorly organized TADs). Default is FALSE. |
| z_clust | Option to filter sub-TADs based on the z-score of their eigenvector gaps. Default is TRUE. |
| eigenvalues | The number of eigenvectors to be calculated. The default and suggested setting is 2. |
| min_size | The minimum allowable TAD size measured in bins. Default is 5. |
| window_size | The size of the sliding window for calculating TADs. Smaller window sizes correspond to less noise from long-range contacts but limit the possible size of TADs |

| | |
|---------------|---|
| resolution | The resolution of the contact matrix. If none selected, the resolution is estimated by taking the most common distance between bins. For $n \times (n+3)$ contact matrices, this value is automatically calculated from the first three columns. |
| gap_threshold | Corresponds to the percentage of zeros allowed before a column/row is removed from the analysis. 1=100%, .7 = 70%, etc. Default is 1. |
| grange | Parameter to determine whether the result should be a GRangeList object. Defaults to FALSE |
| out_format | Specifies the format of the file which SpectralTAD outputs. If "none", no file is output. "juicebox" or "bedpe" returns a bedpe file compatible with juicebox. "hicexplorer" or "bed" returns a bed file compatible with hicexplorer. Default is none |
| out_path | Path of output file. Default is the chromosome |

Details

Given a sparse 3 column, an $n \times n$ contact matrix, or $n \times (n+3)$ contact matrix, SpectralTAD returns a list of TAD coordinates in BED format. SpectralTAD works by using a sliding window that moves along the diagonal of the contact matrix. By default, we use the biologically relevant maximum TAD size of 2Mb and minimum size of 5 bins to determine the size of this window. Within each window, we calculate a Laplacian matrix and determine the location of TAD boundaries based on gaps between eigenvectors calculated from this matrix. The number of TADs in a given window is calculated by finding the number that maximizes the silhouette score. A hierarchy of TADs is created by iteratively applying the function to sub-TADs. The number of levels in each hierarchy is determined by the user.

Value

A list where each entry is in BED format corresponding to the level of the hierarchy.

Examples

```
#Read in data
data("rao_chr20_25_rep")
#Find TADs
spec_table <- SpectralTAD(rao_chr20_25_rep, chr= 'chr20')
```

SpectralTAD_Par

Parallelized Hierarchical Spectral Clustering of TADs

Description

Parallelized Hierarchical Spectral Clustering of TADs

Usage

```

SpectralTAD_Par(
  cont_list,
  chr,
  levels = 1,
  qual_filter = FALSE,
  z_clust = FALSE,
  eigenvalues = 2,
  min_size = 5,
  window_size = 25,
  resolution = "auto",
  grange = FALSE,
  gap_threshold = 1,
  cores = "auto",
  labels = NULL
)

```

Arguments

| | |
|---------------|---|
| cont_list | List of contact matrices where each is in either sparse 3 column, $n \times n$ or $n \times (n+3)$ form, where the first 3 columns are chromosome, start and end coordinates of the regions. If an $n \times n$ matrix is used, the column names must correspond to the start point of the corresponding bin. Required. |
| chr | Vector of chromosomes in the same order as their corresponding contact matrices. Must be same length as cont_list. Required. |
| levels | The number of levels of the TAD hierarchy to be calculated. The default setting is 1. |
| qual_filter | Option to turn on quality filtering which removes TADs with negative silhouette scores (poorly organized TADs). Default is FALSE. |
| z_clust | Option to filter sub-TADs based on the z-score of their eigenvector gaps. Default is TRUE. |
| eigenvalues | The number of eigenvectors to be calculated. The default and suggested setting is 2. |
| min_size | The minimum allowable TAD size measured in bins. Default is 5. |
| window_size | The size of the sliding window for calculating TADs. Smaller window sizes correspond to less noise from long-range contacts but limit the possible size of TADs |
| resolution | The resolution of the contact matrix. If none selected, the resolution is estimated by taking the most common distance between bins. For $n \times (n+3)$ contact matrices, this value is automatically calculated from the first 3 columns. |
| grange | Parameter to determine whether the result should be a GRangeList object. Defaults to FALSE |
| gap_threshold | Corresponds to the percentage of zeros allowed before a column/row is removed from analysis. $1=100\%$, $.7 = 70\%$, etc. Default is 1. |
| cores | Number of cores to use. Defaults to total available cores minus one. |

labels Vector of labels used to name each contact matrix. Must be same length as `cont_list`. Default is `NULL`.

Details

This is the parallelized version of the `SpectralTAD()` function. Given a sparse 3 column, an $n \times n$ contact matrix, or $n \times (n+3)$ contact matrix, `SpectralTAD` returns a list of TAD coordinates in BED format. `SpectralTAD` works by using a sliding window that moves along the diagonal of the contact matrix. By default we use the biologically relevant maximum TAD size of 2Mb and minimum size of 5 bins to determine the size of this window. Within each window, we calculate a Laplacian matrix and determine the location of TAD boundaries based on gaps between eigenvectors calculated from this matrix. The number of TADs in a given window is calculated by finding the number that maximize the silhouette score. A hierarchy of TADs is created by iteratively applying the function to sub-TADs. The number of levels in each hierarchy is determined by the user.

Value

List of lists where each entry is a list of data frames or `GRanges` in BED format corresponding to TADs separated by hierarchies

Examples

```
#Read in data
data("rao_chr20_25_rep")
#Make a list of matrices
mat_list = list(rao_chr20_25_rep, rao_chr20_25_rep)
#Make a vector of chromosomes
chr = c("chr20", "chr20")
#Make a vector of labels
labels = c("run1", "run2")
spec_table <- SpectralTAD_Par(mat_list, chr= chr, labels = labels, cores = 2)
```

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* **datasets**

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