Package 'TADreg'

May 20, 2021

Type Package

Title Versatile Regression Framework for TAD Analysis and Prediction.

Version 1.0

Depends R (>= 3.6.3)

Imports BSgenome.Mmusculus.UCSC.mm10, rtracklayer, GenomicRanges, glmnet, HiTC, hicrep, Matrix, glmnet, data.table, mgcv, L0Learn, doMC, GenomeInfoDb, IRanges, MASS, S4Vectors

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Description Here, we propose a versatile regression framework which not only identifies TADs in a fast and accurare manner, but also detects differential TAD borders across conditions for which few methods exist, and predicts 3D genome reorganizarion after chromosomal rearrangement. Moreover, the framework is biologically meaningful, has an intuitive interpretation and is easy to visualize.

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NeedsCompilation no

R topics documented:

TADreg-package *Versatile Regression Framework for TAD Analysis and Prediction.*

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Here, we propose a versatile regression framework which not only identifies TADs in a fast and accurare manner, but also detects differential TAD borders across conditions for which few methods exist, and predicts 3D genome reorganizarion after chromosomal rearrangement. Moreover, the framework is biologically meaningful, has an intuitive interpretation and is easy to visualize.

Details

The DESCRIPTION file:

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Maintainer:	Raphael Mourad <raphael.mourad@univ-tlse3.fr>
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License:	MIT License

Index of help topics:

To use TADreg, see the R Markdown html file which shows examples to run the different functions (SIM, DIM and PIM) from the package.

Author(s)

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`CHiC_Epha4_DelB_E115_HTCexp` *Capture-Hi-C matrix in DelB/DelB mouse limb buds.*

Description

This is an Hi-C matrix at EPHA4 locus (Chr1:73-79Mb) in HTCexp format (HiTC R package) from the article of Bianco et al, Nature Genetics 2018.

Usage

```
data(CHiC_Epha4_DelB_E115_HTCexp)
```

Author(s)

Raphael Mourad

References

Bianco, S., Lupiáñez, D. G., Chiariello, A. M., Annunziatella, C., Kraft, K., Schöpflin, R., Wittler, L., Andrey, G., Vingron, M., Pombo, A., Mundlos, S., and Nicodemi, M. (April, 2018) Polymer physics predicts the effects of structural variants on chromatin architecture. Nature Genetics, 50(5), 662–667.

`CHiC_Epha4_WT_E115_HTCexp` *Capture-Hi-C matrix in wild-type mouse limb buds.*

Description

This is an Hi-C matrix at EPHA4 locus (Chr1:73-79Mb) in HTCexp format (HiTC R package) from the article of Bianco et al, Nature Genetics 2018.

Usage

```
data(CHiC_Epha4_WT_E115_HTCexp)
```

Author(s)

Raphael Mourad

References

Bianco, S., Lupiáñez, D. G., Chiariello, A. M., Annunziatella, C., Kraft, K., Schöpflin, R., Wittler, L., Andrey, G., Vingron, M., Pombo, A., Mundlos, S., and Nicodemi, M. (April, 2018) Polymer physics predicts the effects of structural variants on chromatin architecture. Nature Genetics, 50(5), 662–667.

`compSCC` *Simple function to compute the stratum adjusted correlation (SCC) between two Hi-C matrices.*

Description

It is useful for benchmarking to compare the observed Hi-C matrix after chromosomal rearrangement and the predicted Hi-C matrix computed using PIM function. An SCC close to one means that predictions of rearranged 3D genome are accurate compared to observed Hi-C data from rearranged 3D genome. An SCC close to zero means the predictions are very inaccurate. Compared to the classical Pearson or Spearson correlation coefficients, SCC removes the distance effect from the Hi-C matrices, allowing to focus on the biological variability, here TADs, sub-TADs, hierarchies of TADs, loops, etc.

Usage

```
compSCC(HTC1, HTC2)
```

Arguments

`HTC1`	Observed Hi-C matrix, for a particular chromosome. It should be stored as an HTCexp object from HiTC R package.
`HTC2`	Predicted Hi-C matrix from PIM function, for a particular chromosome. It should be stored as an HTCexp object from HiTC R package.

Value

The stratum adjusted correlation value.

Author(s)

Raphael Mourad

DIM *Differential Insulation Model (DIM)*

Description

Differential Insulation Model (DIM) is a regression model used to identify differential TAD borders between two different Hi-C experiment matrices (e.g. between two conditions).

Usage

```
DIM(HTC1, HTC2, distMax = NULL, analysis = "border", overlap = 1)
```

Arguments

HTC1	Hi-C matrix from the first condition, for a particular chromosome. It should be stored as an HTCexp object from HiTC R package.
HTC2	Hi-C matrix from the second condition, for the same particular chromosome. It should be stored as an HTCexp object from HiTC R package.
distMax	The maximal distance between two bins that is used to identify TADs. Usually, a distance equal to 10 bins is fine (default value). Setting a too high maximal distance will lead to computational burden.
analysis	If analysis = "border" (default), differential TAD borders will be assessed. If analysis = "facilitator", differential TAD facilitators will be assessed.
overlap	To prevent bin uncertainty between conditions (for instance bin i is identified as a border in condition 1 and bin i+1 is found as border in condition 2), only one bin among two consecutive bins was kept (overlap = 1). This avoids considering as differential border two consecutive bins from two conditions (likely a false positive).

Value

A GRanges object containing the bin genomic coordinates and the corresponding beta values. Bins with beta.diff < 0 correspond to TAD borders that are gained/reinforced in the second condition compared to the first condition, whereas bins with beta.diff > 0 correspond to TAD borders that are lost/weakened in the second condition compared to the first condition.

Author(s)

Raphael Mourad

HiC_CN_mouse_HTCexp *Hi-C matrix in mouse cortical neurons.*

Description

This is an Hi-C matrix for chr18 (50-70 Mb) in HTCexp format (HiTC R package) from the article of Bonev et al, Cell 2017.

Usage

```
data(HiC_CN_mouse_HTCexp)
```

Author(s)

Raphael Mourad

References

Bonev, B., Mendelson Cohen, N., Szabo, Q., Fritsch, L., Papadopoulos, G. L., Lubling, Y., Xu, X., Lv, X., Hugnot, J.-P., Tanay, A., and Cavalli, G. (October, 2017) Multiscale 3D genome rewiring during mouse neural development. Cell, 171(3), 557–572.

HiC_ES_mouse_HTCexp *Hi-C matrix in mouse embryonic stem cells.*

Description

This is an Hi-C matrix for chr18 (50-70 Mb) in HTCexp format (HiTC R package) from the article of Bonev et al, Cell 2017.

Usage

```
data(HiC_ES_mouse_HTCexp)
```

Author(s)

Raphael Mourad

References

Bonev, B., Mendelson Cohen, N., Szabo, Q., Fritsch, L., Papadopoulos, G. L., Lubling, Y., Xu, X., Lv, X., Hugnot, J.-P., Tanay, A., and Cavalli, G. (October, 2017) Multiscale 3D genome rewiring during mouse neural development. Cell, 171(3), 557–572.

HTCfromCHICdata — *Function to read capture Hi-C data from Simona Bianco et al. Nat Genet 2018.*

Description

Function used to read capture Hi-C data from the article "Polymer physics predicts the effects of structural variants on chromatin architecture", Simona Bianco et al., Nature Genetics 2018.

Usage

```
HTCfromCHICdata(file_CHIC)
```

Arguments

file_CHIC	The file path to the capture Hi-C data.

Value

A HTCexp object containing the capture Hi-C data.

Author(s)

Raphael Mourad

HTCfromJuicerDump — *Function to read Hi-C data from Juicebox dump.*

Description

First, dump (extract) a Hi-C data matrix from a Juicebox .hic file using Juicebox dump tool (https://github.com/aidenlab/juicer Extraction). Then, use this function HTCfromJuicerDump to load the Hi-C matrix and convert it to HTCexp format.

Usage

```
HTCfromJuicerDump(file_juicer_dump, resolution, chr, assembly, sparse = T)
```

Arguments

file_juicer_dump	File path to the dumped Hi-C matrix.
resolution	Hi-C data matrix resolution (bin size).
chr	Chromosome.
assembly	Genome assembly.
sparse	Whether the dumped Hi-C matrix is in dense (sparse = F) or sparse format (sparse = F).

Value

The corresponded Hi-C matrix stored as an HTCexp object from HiTC R package.

PIM *Prediction Insulation Model (PIM)*

Description

Prediction Insulation Model (PIM) is a regression model used to predict 3D genome reorganization after a chromosomal rearrangement.

Usage

```
PIM(HTC, structVar.GR, typeVar, output = "asMutant", model = "glmlasso",
distMax = 5e+05, parallel = T, noise = 0)
```

Arguments

HTC	A wild-type Hi-C matrix (no chromosomal rearrangement) for a particular chromosome. It should be stored as an HTCexp object from HiTC R package. Here to improve predictions, you might prefer to focus on a particular region surrounding the chromosomal rearrangement coordinates (for instance -/+10 bins around), and not to give as input the whole chromosomal matrix.
structVar.GR	The chromosomal rearrangement coordinates, stored a GRanges object. It should be larger than a bin (ideally > 5 bins).
typeVar	The type of chromosomal rearrangement : "deletion" or "inversion".
output	The output matrix format. If output = "asMutant", it means that the predicted Hi-C matrix will have modified genomic bins due to the chromosomal rearrangement. If output = "asWT", it means that the predicted Hi-C matrix will have the same genomic bins as the original wild-type Hi-C matrix.
model	By default, the model = "glmlasso" should be used. Other models produce less accurate predictions.
distMax	The maximal distance between two bins that is used to identify TADs. Here to improve predictions, if you used as suggested above only a Hi-C matrix corresponding to a particular region surrounding the chromosomal rearrangement, then it should be better to run computations on a large distance.
parallel	If parallel = True, parallel computing will be done on multiple cores using the parallel R library.
noise	By default, noise is not added to the predicted Hi-C matrix (noise = 0). But one can add some noise (noise > 0) to mimic experimental Hi-C data.

Value

A predicted Hi-C matrix after chromosomal rearrangement for a particular chromosome. It is stored as an HTCexp object from HiTC R package.

Author(s)

Raphael Mourad

SIM *Sparse Insulation Model (SIM)*

Description

Sparse Insulation Model (SIM) is a regression model that is used to map topologically associating domain (TAD) borders and facilitators. TADs are defined as regions in-between two consecutive TAD borders. SIM is based on a regression framework that generalizes the insulation score by estimating a relative score and adding a sparsity constrain.

Usage

```
SIM(HTC, distMax = NULL, penalty = "L0", prefilter = T)
```

Arguments

HTC	A Hi-C matrix for a particular chromosome. It should be stored as an HTCexp object from HiTC R package.
distMax	The maximal distance between two bins that is used to identify TADs. Usually a distance equal to 10 bins is fine (default value). Setting a too high maximal distance will lead to computational burden.
penalty	The penalty (regularization) applied to the regression estimation: "none" (no penalty, classical regression), "L1" (lasso regression) and "L0" (default: L0 regression).
prefilter	If the number of bins in the matrix is too big (eg > 2000), the L0 regression might fail to process all the bins (variables), due to computational burden. In this case, one can use a prefilter step based on lasso regression to remove bins with abs(betas)<0.2, and then to run L1 regression. Used by default.

Value

A GRanges object containing the Hi-C bin genomic coordinates and the corresponding beta values. Bins with betas < 0 correspond to TAD borders, whereas bins with betas > 0 correspond to TAD facilicators.

Author(s)

Raphael Mourad

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