

Package ‘cellscape’

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Title Explores single cell copy number profiles in the context of a single cell tree

Version 1.31.0

Description CellScape facilitates interactive browsing of single cell clonal evolution datasets. The tool requires two main inputs: (i) the genomic content of each single cell in the form of either copy number segments or targeted mutation values, and (ii) a single cell phylogeny. Phylogenetic formats can vary from dendrogram-like phylogenies with leaf nodes to evolutionary model-derived phylogenies with observed or latent internal nodes. The CellScape phylogeny is flexibly input as a table of source-target edges to support arbitrary representations, where each node may or may not have associated genomic data. The output of CellScape is an interactive interface displaying a single cell phylogeny and a cell-by-locus genomic heatmap representing the mutation status in each cell for each locus.

License GPL-3

Depends R (>= 3.3)

Imports dplyr (>= 0.4.3), gtools (>= 3.5.0), htmlwidgets (>= 0.5), jsonlite (>= 0.9.19), reshape2 (>= 1.4.1), stringr (>= 1.0.0)

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Description

cellscape explores single cell copy number profiles in the context of a single cell phylogeny.

Usage

```
cellscape(
  cnv_data = NULL,
  mut_data = NULL,
  mut_data_matrix = NULL,
  mut_order = NULL,
  tree_edges,
  gtype_tree_edges = NULL,
  sc_annot = NULL,
  clone_colours = "NA",
  timepoint_title = "Timepoint",
  clone_title = "Clone",
  xaxis_title = "Time Point",
  yaxis_title = "Clonal Prevalence",
  phylogeny_title = "Clonal Phylogeny",
  value_type = NULL,
  node_type = "Cell",
  display_node_ids = FALSE,
  prop_of_clone_threshold = 0.2,
  vaf_threshold = 0.05,
  show_warnings = TRUE,
  width = 900,
  height = 800
)
```

Arguments

cnv_data	<p>data.frame (Required if not providing mut_data nor mut_data_matrix) Single cell copy number segments data. Note that every single cell id must be present in the tree_edges data frame. Required columns are:</p> <p>single_cell_id: character() single cell id. chr: character() chromosome number. start: numeric() start position. end: numeric() end position. copy_number: numeric() copy number state.</p>
mut_data	<p>data.frame (Required if not providing cnv_data nor mut_data_matrix) Single cell targeted mutation data frame. Note that every single cell id must be present in the tree_edges data frame. Required columns are:</p> <p>single_cell_id: character() single cell id. chr: character() chromosome number. coord: numeric() genomic coordinate. VAF: numeric() variant allele frequency [0, 1].</p>
mut_data_matrix	<p>matrix (Required if not providing cnv_data nor mut_data) Single cell targeted mutation matrix. Rows are single cell IDs, columns are mutations. Rows and columns must be named, column names in the format "<chromosome>:<coordinate>". Note that the order of these rows and columns will not be preserved, unless mutation order is the same as that specified in the mut_order parameter. Also note that every single cell id must be present in the tree_edges data frame.</p>
mut_order	<p>vector (Optional) Mutation order for targeted mutation heatmap (each mutation should consist of a string in the form "chrom:coord"). Default will use a clustering function to determine mutation order.</p>
tree_edges	<p>data.frame Edges for the single cell phylogenetic tree. Required columns are:</p> <p>source: character() edge source (single cell id). target: character() edge target (single cell id).</p> <p>Optional columns are:</p> <p>dist: numeric() edge distance.</p>
gtype_tree_edges	<p>data.frame (Required for TimeScape) Genotype tree edges of a rooted tree. Required columns are:</p> <p>source: character() source node id. target: character() target node id.</p>
sc_annot	<p>data.frame (Required for TimeScape) Annotations (genotype and sample id) for each single cell. Required columns are:</p> <p>single_cell_id: character() single cell id. genotype: character() genotype assignment.</p> <p>Optional columns are:</p> <p>timepoint: character() id of the sampled time point. Note: time points will be ordered alphabetically.</p>

clone_colours	data.frame (Optional) Clone ids and their corresponding colours (in hex format). Required columns are: clone_id: character() clone id. colour: character() the corresponding Hex colour for each clone id.
timepoint_title	character() (Optional) Legend title for timepoint groups. Default is "Timepoint".
clone_title	character() (Optional) Legend title for clones. Default is "Clone".
xaxis_title	character() (Optional) For TimeScape - x-axis title. Default is "Time Point".
yaxis_title	character() (Optional) For TimeScape - y-axis title. Default is "Clonal Prevalence".
phylogeny_title	character() (Optional) For TimeScape - legend phylogeny title. Default is "Clonal Phylogeny".
value_type	character() (Optional) The type of value plotted in heatmap - will affect legend and heatmap tooltips. Default is "VAF" for mutation data, and "CNV" for copy number data.
node_type	character() (Optional) The type of node plotted in single cell phylogeny - will affect phylogeny tooltips. Default is "Cell".
display_node_ids	logical() (Optional) Whether or not to display the single cell ID within the tree nodes. Default is FALSE.
prop_of_clone_threshold	numeric() (Optional) Used for the ordering of targeted mutations. The minimum proportion of a clone to have a mutation in order to consider the mutation as present within that clone. Default is 0.2.
vaf_threshold	numeric() (Optional) Used for the ordering of targeted mutations. The minimum variant allele frequency for a mutation to be considered as present within a single cell. Default is 0.05.
show_warnings	logical() (Optional) Whether or not to show any warnings. Default is TRUE.
width	numeric() (Optional) Width of the plot.
height	numeric() (Optional) Height of the plot.

Details

Interactive components:

1. Mouseover any single cell in the phylogeny to view its corresponding genomic profile in the heatmap, and vice versa.
2. Mouseover any part of the heatmap to view the CNV or VAF value for that copy number segment or mutation site, respectively.
3. Mouseover any branch of the phylogeny to view downstream single cells, both in the phylogeny and heatmap.
4. Mouseover any clone to view its corresponding single cells in the phylogeny and heatmap.

5. Click any node in the phylogeny to flip the order of its descendant branches.
6. Use the selection tool in the tool bar to select single cell genomic profiles and view their corresponding single cells in the phylogeny.
7. Use the tree trimming tool in the tool bar to remove any branch of the phylogeny by clicking it.
8. Use the switch view tool in the tool bar to change the phylogeny view from force-directed to unidirectional, and vice versa.
9. Use the re-root phylogeny tool to root the phylogeny at a clicked node.
10. Use the flip branch tool to vertically rotate any branch by clicking its root node.
11. If present, use the scale tree/graph tool in the tool bar to scale the phylogeny by the provided edge distances.
12. If time-series information is present such that the TimeScope is displayed below the CellScape, clones and time points are interactively linked in both views on mouseover.
13. Click the download buttons to download a PNG or SVG of the view.

Note:

See TimeScope repo (https://bitbucket.org/MO_BCCRC/timescape) for more information about TimeScope.

Examples

```
library("cellscape")

# EXAMPLE 1 - TARGETED MUTATION DATA

# single cell tree edges
tree_edges <- read.csv(system.file("extdata", "targeted_tree_edges.csv",
  package = "cellscape"
))

# targeted mutations
targeted_data <- read.csv(system.file("extdata", "targeted_muts.csv",
  package = "cellscape"
))

# genotype tree edges
gtype_tree_edges <- data.frame("source" = c(
  "Ancestral", "Ancestral", "B",
  "C", "D"
), "target" = c("A", "B", "C", "D", "E"))

# annotations
sc_annot <- read.csv(system.file("extdata", "targeted_annots.csv",
  package = "cellscape"
))

# mutation order
```

```

mut_order <- scan(system.file("extdata", "targeted_mut_order.txt",
  package = "cellscape"
), what = character())

# run cellscape
cellscape(
  mut_data = targeted_data, tree_edges = tree_edges, sc_annot =
  sc_annot, gtype_tree_edges = gtype_tree_edges, mut_order = mut_order
)

# EXAMPLE 2 - COPY NUMBER DATA

# single cell tree edges
tree_edges <- read.csv(system.file("extdata", "cnv_tree_edges.csv",
  package = "cellscape"
))

# cnv segments data
cnv_data <- read.csv(system.file("extdata", "cnv_data.csv",
  package =
  "cellscape"
))

# annotations
sc_annot <- read.csv(system.file("extdata", "cnv_annots.tsv",
  package =
  "cellscape"
), sep = "\t")

# custom clone colours
clone_colours <- data.frame(
  clone_id = c("1", "2", "3"),
  colour = c("7fc97f", "beaed4", "fdc086")
)

# run cellscape
cellscape(
  cnv_data = cnv_data, tree_edges = tree_edges, sc_annot = sc_annot,
  width = 800, height = 475, show_warnings = FALSE,
  clone_colours = clone_colours
)

```

dfs_tree

Get depth first search of a tree

Description

Get depth first search of a tree

Widget output function for use in Shiny

Widget render function for use in Shiny
Function to get data frame of pixels
function to get min and max values for each chromosome
function to get chromosome box pixel info
function to get the genome length
function to get the number of base pairs per pixel
function to get information (chr, start, end, mode_cnv) for each pixel
function to get mutation order for targeted data
function to get targeted heatmap information
function to find the mode of a vector
Function to process the user data
Function to check minimum dimensions
Function to check required inputs are present
check alpha value input is correct
check clonal_prev parameter data
check tree_edges parameter data
check genotype_position parameter
check clone_colours parameter
check perturbations parameter
get mutation data
function to replace spaces with underscores in all data frames & keep maps of original names to space-replaced names

Usage

```
dfs_tree(edges, cur_root, dfs_arr)

cellscapeOutput(outputId, width = "100%", height = "400px")

renderCnvTree(expr, env = parent.frame(), quoted = FALSE)

getEmptyGrid(hm_sc_ids_ordered, ncols)

getChromBounds(chroms, cnv_data)

getChromBoxInfo(chrom_bounds, n_bp_per_pixel)

getGenomeLength(chrom_bounds)

getNBPPerPixel(ncols, chrom_bounds, genome_length)

getCNVHeatmapForEachSC(cnv_data, chrom_bounds, n_bp_per_pixel)
```

```
getMutOrder(mut_data)

getTargetedHeatmapForEachSC(mut_data, mut_order, heatmapWidth)

findMode(x)

processUserData(
  clonal_prev,
  tree_edges,
  mutations,
  clone_colours,
  xaxis_title,
  yaxis_title,
  phylogeny_title,
  alpha,
  genotype_position,
  perturbations,
  sort,
  show_warnings,
  width,
  height
)

checkMinDims(mutations, height, width)

checkRequiredInputs(clonal_prev, tree_edges)

checkAlpha(alpha)

checkClonalPrev(clonal_prev)

checkTreeEdges(tree_edges)

checkGtypePositioning(genotype_position)

checkCloneColours(clone_colours)

checkPerts(perturbations)

getMutationsData(mutations, tree_edges, clonal_prev, show_warnings = TRUE)

replaceSpaces(
  clonal_prev,
  tree_edges,
  clone_colours,
  mutation_info,
  mutations,
```



```

    mutation_prevalences
)

```

Arguments

edges – edges of tree

cur_root – current root of the tree

dfs_arr – array of depth first search results to be filled

outputId – id of output

width – width provided by user

height – height provided by user

expr – expression for Shiny

env – environment for Shiny

quoted – default is FALSE

hm_sc_ids_ordered – array of single cell ids in order

ncols – integer of number of columns (pixels) to fill

chroms – vector of chromosome names

cnv_data – data frame of copy number variant segments data

chrom_bounds – data frame of chromosome boundaries

n_bp_per_pixel – integer of number of base pairs per pixel

genome_length – integer of length of the genome

mut_data – data frame of mutations data

mut_order – array of order of mutations for heatmap (chromosome:coordinate)

heatmapWidth – number for width of the heatmap (in pixels)

x – vector of numbers

clonal_prev – clonal_prev data from user

tree_edges – tree edges data from user

mutations – mutations data from user

clone_colours – clone_colours data from user

xaxis_title – String (Optional) of x-axis title. Default is "Time Point".

yaxis_title – String (Optional) of y-axis title. Default is "Clonal Prevalence".

phylogeny_title – String (Optional) of Legend phylogeny title. Default is "Clonal Phylogeny".

alpha – alpha provided by user

genotype_position – genotype_position provided by user

perturbations – perturbations provided by user

sort – Boolean (Optional) of whether (TRUE) or not (FALSE) to vertically sort the genotypes by their emergence values (descending). Default is FALSE. Note that genotype sorting will always retain the phylogenetic hierarchy, and this parameter will only affect the ordering of siblings.

show_warnings – Boolean (Optional) of Whether or not to show any warnings. Default is TRUE.

mutation_info – processed mutation_info

mutation_prevalences – mutation_prevalences data from user

Examples

```

dfs_tree(
  data.frame(
    source = c("1", "1", "2", "2", "5", "6"),
    target = c("2", "5", "3", "4", "6", "7")
  ), "1", c()
)
cellscapeOutput(1, "100%", "300px")
cellscapeOutput(1, "80%", "300px")
findMode(c(1, 1, 19, 1))
checkMinDims(data.frame(chr = c("11"), coord = c(104043), VAF = c(0.1)), "700px", "700px")
checkRequiredInputs(
  data.frame(
    timepoint = c(rep("Diagnosis", 6), rep("Relapse", 1)),
    clone_id = c("1", "2", "3", "4", "5", "6", "7"),
    clonal_prev = c("0.1", "0.22", "0.08", "0.53", "0.009", "0.061", "1")
  ),
  data.frame(
    source = c("1", "1", "2", "2", "5", "6"),
    target = c("2", "5", "3", "4", "6", "7")
  )
)
checkRequiredInputs(
  data.frame(
    timepoint = c(rep("Diagnosis", 6), rep("Relapse", 1)),
    clone_id = c("1", "2", "3", "4", "5", "6", "7"),
    clonal_prev = c("0.12", "0.12", "0.18", "0.13", "0.009", "0.061", "1")
  ),
  data.frame(
    source = c("1", "1", "2", "2", "5", "6"),
    target = c("2", "5", "3", "4", "6", "7")
  )
)
checkAlpha(4)
checkAlpha(100)
checkClonalPrev(data.frame(timepoint = c(1), clone_id = c(2), clonal_prev = c(0.1)))
checkTreeEdges(
  data.frame(
    source = c("1", "1", "2", "2", "5", "6"),
    target = c("2", "5", "3", "4", "6", "7")
  )
)

```

```

)
checkGtypePositioning("centre")
checkCloneColours(
  data.frame(
    clone_id = c("1", "2", "3", "4"),
    colour = c("#beaed4", "#fdc086", "#beaed4", "#beaed4")
  )
)
)
checkPerts(data.frame(pert_name = c("New Drug"), prev_tp = c("Diagnosis")))
getMutationsData(
  data.frame(
    chrom = c("11"), coord = c(104043), VAF = c(0.1),
    clone_id = c(1), timepoint = c("Relapse")
  ),
  data.frame(
    source = c("1", "1", "2", "2", "5", "6"),
    target = c("2", "5", "3", "4", "6", "7")
  ),
  data.frame(
    timepoint = c(rep("Diagnosis", 6), rep("Relapse", 1)),
    clone_id = c("1", "2", "3", "4", "5", "6", "7"),
    clonal_prev = c("0.12", "0.12", "0.18", "0.13", "0.009", "0.061", "1")
  )
)
)
replaceSpaces(
  mutations = data.frame(
    chrom = c("11"), coord = c(104043),
    VAF = c(0.1), clone_id = c(1), timepoint = c("Relapse")
  ),
  tree_edges = data.frame(
    source = c("1", "1", "2", "2", "5", "6"),
    target = c("2", "5", "3", "4", "6", "7")
  ),
  clonal_prev = data.frame(
    timepoint = c(rep("Diagnosis", 6), rep("Relapse", 1)),
    clone_id = c("1", "2", "3", "4", "5", "6", "7"),
    clonal_prev = c("0.12", "0.12", "0.18", "0.13", "0.009", "0.061", "1")
  ),
  mutation_prevalences = list(
    "X:6154028" = data.frame(timepoint = c("Diagnosis"), VAF = c(0.5557))
  ),
  mutation_info = data.frame(clone_id = c(1)),
  clone_colours = data.frame(
    clone_id = c("1", "2", "3", "4"),
    colour = c("#beaed4", "#fdc086", "#beaed4", "#beaed4")
  )
)
)
)

```

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