Package 'SpliceImpactR'

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Type Package

Title An R package to identify functional impacts due to alternative RNA processing events

Version 0.99.4

Description Works by taking in processed data from the HIT Index and/or rMATS and identifying how differentially used alternative RNA processing events lead to changes in protein function through various means. Primarily this is done through protein similarity, functional protein domain analysis, and domain-domain interaction changes. Notably, we both identify alterantive RNA processing event 'swaps' across condition and are able to perform holistic analyses regarding the impact of different RNA processing events.

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.coords_to_string_1b *Combine start/end coordinates into "start-end" strings (1-based).*

Description

Combine start/end coordinates into "start-end" strings (1-based).

Usage

```
.coords_to_string_1b(start, end)
```

Arguments

`start`, `end`	Integer vectors of equal length.

Value

Character vector of "start-end" strings (NA for invalid pairs).

.db_remove_domain *Removes the part of a domain identifier after the first semicolon.*

Description

Removes the part of a domain identifier after the first semicolon.

Usage

```
.db_remove_domain(id)
```

Arguments

`id`	Character vector of domain identifiers (e.g. ‘"Pfam;Kinase"‘).

Value

Character vector containing only the database name (e.g. ‘"Pfam"‘).

`.domain_remove_db` *Removes the database portion from a semicolon-delimited domain ID.*

Description

Removes the database portion from a semicolon-delimited domain ID.

Usage

```
.domain_remove_db(id)
```

Arguments

`id`	Character vector of domain identifiers (e.g. ‘"Pfam;Kinase"‘).

Value

Character vector of domain names (e.g. ‘"Kinase"‘).

`.find_hitindex_files` *Locate HIT index PSI files within a directory or return the file if directly provided.*

Description

Locate HIT index PSI files within a directory or return the file if directly provided.

Usage

```
.find_hitindex_files(p)
```

Arguments

`p`	Directory path or file path.

Value

Character vector of full paths to matching files.

.getHITindex *Read HIT index exon tables for all samples*

Description

Internal helper that loads exon-level HIT index tables for each sample and appends corresponding ‘sample_name‘ and ‘condition‘ metadata.

Usage

```
.getHITindex(sample_df)
```

Arguments

sample_df ‘data.frame‘ or ‘data.table‘ containing at least:

- ‘path‘ directory path for each sample
- ‘sample_name‘ unique sample identifier
- ‘condition‘ experimental group

Value

A ‘data.table‘ with columns: ‘gene‘, ‘exon‘, ‘HITindex‘, ‘sample‘, and ‘condition‘.

.get_size_factors_from_exons *Compute size factors directly from exon count files*

Description

Wrapper around ‘getSizeFactors()‘ that can either compute normalization factors from raw exon count files (‘exon_files‘) or use user-provided values (‘user_given‘).

Usage

```
.get_size_factors_from_exons(sample_df, method = c("exon_files", "user_given"))
```

Arguments

sample_df ‘data.frame‘ containing sample metadata with columns ‘sample_name‘, ‘path‘, and optionally ‘condition‘.

method Either ‘’exon_files’‘ (compute) or ‘’user_given’‘ (join).

Details

- If ‘method = ’exon_files’‘, the function loads exon-level count tables using ‘.read_exon_files()‘ and computes per-sample size factors. - If ‘method = ’user_given’‘, it merges the user-supplied ‘size_factors‘ data frame into ‘sample_df‘.

Size factors are normalized to have a geometric mean of 1 (DESeq2-style).

Value

A ‘data.frame‘ equal to ‘sample_df‘ with an appended numeric column ‘sizeFactor‘.

See Also

[getSizeFactors()]

`.needs_upstream_check` *Check for upstream frame shift*

Description

‘.needs_upstream_check()‘ indicates whether a given alternative splicing event type should undergo upstream frame-shift evaluation via ‘.incoming_upstream_shift()‘.

Usage

```
.needs_upstream_check(event_type)
```

Arguments

`event_type`	Character scalar or vector. Event class label(s) such as ‘"A5SS"‘, ‘"A3SS"‘, ‘"RI"‘, ‘"SE"‘, ‘"MXE"‘, etc.

Value

Logical vector of same length as input. ‘TRUE‘ for event types where an upstream frame-shift scan is relevant.

`.parse_exon_coords` *Parse exon coordinate strings of form "chr:start-end" into components.*

Description

Parse exon coordinate strings of form "chr:start-end" into components.

Usage

```
.parse_exon_coords(exon_col)
```

Arguments

`exon_col`	Character vector of exon coordinate strings.

Value

A list with elements `chr`, `start`, and `end`.

`.parse_listcol` *Internal helper that normalizes list columns or delimited strings of domain identifiers into unique trimmed character vectors.*

Description

Internal helper that normalizes list columns or delimited strings of domain identifiers into unique trimmed character vectors.

Usage

```
.parse_listcol(x, delim = "[,;|[:space:]]+")
```

Arguments

`x`	List or character vector of domain entries.
`delim`	Regular expression used to split delimited strings.

Value

A list of character vectors, one per input element.

.read_any   *Read an object from a supported file format (.rds, .csv, .tsv)*

Description

Internal helper to load serialized or tabular data in a uniform way.

Usage

```
.read_any(path)
```

Arguments

path	Character scalar; path to a file ending in '.rds', '.csv', or '.tsv'.

Value

An R object (data.table, data.frame, or arbitrary R object from '.rds').

.read_exon_files   *Read exon-level counts or annotations used in HIT index files.*

Description

Read exon-level counts or annotations used in HIT index files.

Usage

```
.read_exon_files(path, columns = c("gene", "exon", "ID"))
```

Arguments

path	Base path to HIT index outputs (excluding suffix like ".exon").
columns	Columns to select from the exon file.

Value

A data.table with the specified columns.

`.read_one_hit` *Read and merge a single HIT index PSI file with its exon annotations.*

Description

Read and merge a single HIT index PSI file with its exon annotations.

Usage

```
.read_one_hit(f, sample, condition)
```

Arguments

`f`	Path to a .AFEPSI/.ALEPSI/etc. file.
`sample`	Sample name.
`condition`	Experimental condition.

Value

A standardized data.table with inclusion/exclusion metrics and metadata.

`.site_glm` *Quasi-binomial GLM with Cook's Distance Filtering*

Description

Fits a quasi-binomial GLM to estimate deltaPSI between two conditions. Outliers are removed based on Cook's distance before refitting.

Usage

```
.site_glm(d, cooks_cutoff)
```

Arguments

`d`	A ‘data.frame‘ or ‘data.table‘ with columns ‘psi_adj‘, ‘psi_raw‘, ‘condition‘, and ‘total‘.
`cooks_cutoff`	Numeric. Cook's distance cutoff, passed to [cutoff_num()].

Value

A ‘data.table‘ with columns ‘p.value‘, ‘cooks_max‘, ‘n‘, ‘n_used‘, ‘mean_psi_ctrl‘, ‘mean_psi_case‘, and ‘delta_psi‘.

.si_bfc — *Initialize BiocFileCache backend (internal)*

Description

Initialize BiocFileCache backend (internal)

Usage

```
.si_bfc(base_dir = NULL, pkg = "SpliceImpactR")
```

Arguments

base_dir	Optional cache root passed to [.si_cache_root()].
pkg	Package name used for default user cache root.

Value

A ‘BiocFileCache‘ object.

.si_bfc_get_rds — *Load cached local RDS from BiocFileCache (internal)*

Description

Load cached local RDS from BiocFileCache (internal)

Usage

```
.si_bfc_get_rds(bfc, rname)
```

Arguments

bfc	A ‘BiocFileCache‘ object.
rname	Cache key name.

Value

Cached R object or ‘NULL‘ if not present.

.si_bfc_get_web — *Fetch a web resource through BiocFileCache (internal)*

Description

Fetch a web resource through BiocFileCache (internal)

Usage

```
.si_bfc_get_web(bfc, rname, url, progress = TRUE)
```

Arguments

`bfc`	A ‘BiocFileCache‘ object.
`rname`	Cache key name.
`url`	URL to fetch.
`progress`	Logical passed to BiocFileCache download methods.

Value

Local cached file path.

.si_bfc_put_rds — *Store R object in BiocFileCache as local RDS (internal)*

Description

Store R object in BiocFileCache as local RDS (internal)

Usage

```
.si_bfc_put_rds(bfc, rname, obj)
```

Arguments

`bfc`	A ‘BiocFileCache‘ object.
`rname`	Cache key name.
`obj`	R object to serialize.

Value

Invisible cached file path.

.si_cache_root *Resolve persistent cache root for SpliceImpactR (internal)*

Description

Resolve persistent cache root for SpliceImpactR (internal)

Usage

```
.si_cache_root(base_dir = NULL, pkg = "SpliceImpactR")
```

Arguments

base_dir	Optional directory root for cache data. If ‘NULL‘, defaults to ‘tools::R_user_dir("SpliceImpactR", "cache")‘.
pkg	Package name used by ‘tools::R_user_dir()‘.

Value

Normalized cache root directory path.

.si_gencode_urls *Build GENCODE download URLs (internal helper)*

Description

Internal function to construct URLs for downloading GENCODE annotation and sequence files for either human or mouse. This is used by higher-level SpliceImpactR functions.

Usage

```
.si_gencode_urls(species = c("human", "mouse"), release)
```

Arguments

species	Character string, either ‘"human"‘ or ‘"mouse"‘.
release	Integer or string specifying the GENCODE release number.

Value

A named list containing URLs and the release tag.

`.si_get_annotation_mode_guide` *Build short get_annotation mode/use-case guide (internal)*

Description

Build short get_annotation mode/use-case guide (internal)

Usage

```
.si_get_annotation_mode_guide()
```

Value

Character scalar suitable for appending to error messages.

`.si_link_asset_path` *Resolve optional link-mode asset override (internal)*

Description

Resolve optional link-mode asset override (internal)

Usage

```
.si_link_asset_path(bfc, provided, fallback_path, role)
```

Arguments

`bfc`	A 'BiocFileCache' object.
`provided`	User-supplied override value.
`fallback_path`	Default downloaded asset path.
`role`	Label used in warnings and cache key names.

Value

A valid local file path.

`.si_md5_text` *Compute an MD5 hash for a text payload (internal)*

Description

Compute an MD5 hash for a text payload (internal)

Usage

```
.si_md5_text(txt)
```

Arguments

`txt`	Character scalar payload.

Value

Character scalar MD5 hash.

`.si_pf_cache_key` *Build BiocFileCache key for get_protein_features() outputs (internal)*

Description

Build BiocFileCache key for get_protein_features() outputs (internal)

Usage

```
.si_pf_cache_key(
  biomaRt_databases,
  gtf_df,
  sequences,
  species,
  release,
  combine_overlaps
)
```

Arguments

`biomaRt_databases`	Character vector of requested databases.
`gtf_df`	Annotation table.
`sequences`	Optional sequences table.
`species`	Character species dataset string.
`release`	Ensembl release.
`combine_overlaps`	Logical merge behavior.

Value

Character cache key.

`.si_pf_fingerprint_gtf` *Build a stable GTF fingerprint for protein-feature caching (internal)*

Description

Build a stable GTF fingerprint for protein-feature caching (internal)

Usage

```
.si_pf_fingerprint_gtf(gtf_df)
```

Arguments

`gtf_df`	Annotation table used by [get_protein_features()].

Value

Character scalar fingerprint hash.

`.si_pf_fingerprint_sequences` *Build a stable sequence fingerprint for ELM-dependent caching (internal)*

Description

Build a stable sequence fingerprint for ELM-dependent caching (internal)

Usage

```
.si_pf_fingerprint_sequences(sequences)
```

Arguments

`sequences`	Sequence table from [get_annotation()].

Value

Character scalar fingerprint hash.

.si_prepare_assets *Prepare GENCODE annotation and sequence assets (internal helper)*

Description

Internal function to acquire GENCODE annotation and sequence files (GTF, transcript FASTA, protein FASTA) using a package-specific ‘BiocFileCache‘.

Usage

```
.si_prepare_assets(
  base_dir,
  species = c("human", "mouse"),
  release,
  mode = c("download", "import_then_cache"),
  use_rds_cache = TRUE
)
```

Arguments

base_dir	Character string giving the base directory where cache data should be stored. If ‘NULL‘, uses package user cache.
species	Character string, either ‘"human"‘ or ‘"mouse"‘.
release	Integer or string specifying the GENCODE release number (e.g., ‘45‘ for human or ‘"M35"‘ for mouse).
mode	Character string, one of ‘"download"‘ or ‘"import_then_cache"‘. The latter may parse/cache the GTF R object.
use_rds_cache	Logical; if ‘TRUE‘, loads cached ‘.rds‘ GTF file if available.

Value

A list containing:

‘paths‘ Local file paths to cached assets.

‘gtf_df‘ Imported GTF data frame if loaded or created.

‘meta‘ Metadata list with species, release, and tag.

‘bfc‘ ‘BiocFileCache‘ instance used for retrieval.

‘cache_dir‘ Resolved cache root directory.

.si_use_ensembl_mart — *Create a biomaRt Ensembl connection with explicit mirror fallback (internal)*

Description

Create a biomaRt Ensembl connection with explicit mirror fallback (internal)

Usage

```
.si_use_ensembl_mart(
  dataset,
  version,
  biomart = "genes",
  ensembl_mirror = NULL,
  verbose = FALSE
)
```

Arguments

`dataset`	Ensembl dataset (e.g. ‘"hsapiens_gene_ensembl"‘).
`version`	Ensembl release version.
`biomart`	Biomart name, default ‘"genes"‘.
`ensembl_mirror`	Optional mirror (‘"www"‘, ‘"useast"‘, ‘"asia"‘).
`verbose`	Logical passed to ‘biomaRt::useEnsembl()‘.

Value

A ‘Mart‘ object.

.split_coord — *Split genomic coordinate strings into integer ranges*

Description

Internal helper that converts a string like ‘"12345-12456"‘ into an integer vector ‘c(12345, 12456)‘.

Usage

```
.split_coord(coord)
```

Arguments

`coord`	Character scalar of the form ‘"start-end"‘.

Value

Integer vector of length two (‘start‘, ‘end‘).

`.tail_coords_1based` *Compute 1-based coordinates for the tail segment when one interval fully overlaps another but differs at exactly one boundary (start or end).*

Description

Compute 1-based coordinates for the tail segment when one interval fully overlaps another but differs at exactly one boundary (start or end).

Usage

```
.tail_coords_1based(longS, longE, shortS, shortE)
```

Arguments

`longS`	Integer vector of start coordinates for the longer interval.
`longE`	Integer vector of end coordinates for the longer interval.
`shortS`	Integer vector of start coordinates for the shorter interval.
`shortE`	Integer vector of end coordinates for the shorter interval.

Details

For intervals sharing either their start or end but not both, returns the coordinates of the extra tail portion on the longer interval. Invalid or negative-length intervals are returned as ‘NA‘.

Value

A list with integer vectors:

`start`	1-based start positions of the tail region.
`end`	1-based end positions of the tail region.

.write_any — *Write an object to a supported file format (.rds, .csv, .tsv)*

Description

Internal helper to save serialized or tabular data in a uniform way.

Usage

```
.write_any(dt, path)
```

Arguments

`dt`	Object to save (typically a data.frame or data.table).
`path`	Character scalar; output file path ending in '.rds', '.csv', or '.tsv'.

Value

Invisibly returns the output file path.

add_exon_coding_information — *Add per-exon coding and feature coordinates (internal)*

Description

Internal helper to annotate each exon in a GTF `data.table` with strand-aware coding information. For every exon, the function records whether it overlaps coding sequence (CDS), untranslated region (UTR), start codon, or stop codon, together with absolute, genomic, and transcript-relative coordinates.

Usage

```
add_exon_coding_information(gtf_df)
```

Arguments

`gtf_df`	A `data.frame` or `data.table` containing GTF annotations, typically produced by [load_gtf_long()]. Must include columns `type`, `start`, end, `strand`, `transcript_id`, `exon_id`, and a unique `row_uid`.

Details

The function:

1. Orders exons per transcript, respecting strand.
2. Computes exon-wise coordinates for CDS, UTR, start/stop codons.
3. Merges these annotations back into the exon-level GTF table.

It relies on **data.table** joins and by-group operations for speed.

Value

A `data.table` identical to the input `gtf_df` but with additional per-exon fields:

- `cds_has`, `utr_has`, etc logical indicators
- Absolute (within-exon) start/stop coordinates (`_abs_*`)
- Genomic coordinates (`_gen_*`)
- Transcript-relative coordinates (`_rel_*`)
- Feature lengths (`_len`)

---

add_exon_count_per_transcript

Add exon count per transcript (internal)

Description

Internal helper that computes the number of exon entries per transcript in a GTF table and attaches it as a new column.

Usage

```
add_exon_count_per_transcript(gtf_df, col = "n_exons")
```

Arguments

`gtf_df`	A `data.frame` or `data.table` containing at least `type == "exon"` and `transcript_id` columns.
`col`	Character string giving the name of the output column for the exon count (default `"n_exons"`).

Value

A `data.table` identical to `gtf_df` but with one additional column containing the number of exons per transcript.

`add_exon_frames` *Add frames to exons dependent on cds location*

Description

Internal helper

Usage

```
add_exon_frames(gtf_df)
```

Arguments

`gtf_df` A `data.frame` or `data.table` containing GTF annotation data, typically from [load_gtf_long()].

Value

A `data.table` with added start_frame and stop_frame

`add_exon_order_information` *Add exon order and positional classification (internal)*

Description

Internal helper that annotates exon rows within a GTF table with strand-aware order and coding position information. Adds both absolute (by transcript) and coding-region-specific ordering, along with classification labels such as `"first"`, `"internal"`, `"last"`, or `"single_exon"`.

Usage

```
add_exon_order_information(gtf_df)
```

Arguments

`gtf_df` A `data.frame` or `data.table` containing GTF annotations (usually from [add_exon_coding_information Must include columns `type`, `start`, `end`, `strand`, `transcript_id`, `exon_number`, `cds_has`, and `cds_rel_start`.

Details

Exons are ordered by genomic position within each transcript, taking strand into account. If `exon_number` is provided, it is used to set the absolute order; otherwise order is inferred from coordinates.

Value

A `data.table` identical to `gtf_df` but with added columns:

- `absolute_exon_position` exon index by transcript
- `coding_exon_position` exon index among coding exons
- `absolute_exon_class` positional label for all exons
- `coding_exon_class` positional label for coding exons

`add_feature_length` *Add feature length column (internal)*

Description

Internal helper that computes the genomic length of each feature in a GTF table and appends it as `feature_length`.

Usage

```
add_feature_length(gtf_df)
```

Arguments

`gtf_df`	A `data.frame` or `data.table` containing `start` and `end` columns.

Value

A `data.table` identical to the input but with an added `feature_length` column (`end - start + 1`).

`add_splice_part` *Add one part to an existing SpliceImpactResult*

Description

Add one part to an existing SpliceImpactResult

Usage

```
add_splice_part(
  obj,
  data = NULL,
  res = NULL,
  res_di = NULL,
  matched = NULL,
  sample_frame = NULL,
  hits_final = NULL
)
```

Arguments

`obj`	‘SpliceImpactResult‘
`data`	Optional raw sample-level table.
`res`	Optional differential result table.
`res_di`	Optional threshold-filtered differential table.
`matched`	Optional annotation-matched table.
`sample_frame`	Optional sample manifest table.
`hits_final`	Optional paired/final hits table.

Value

Updated ‘SpliceImpactResult‘

Examples

```
obj <- as_splice_impact_result()
res <- data.table::data.table(
  event_id = c("E1", "E1"),
  form = c("inc", "exc"),
  inc = c("100-110", "120-130"),
  exc = c("120-130", "100-110"),
  chr = c("chr1", "chr1"),
  strand = c("+", "+"),
  gene_id = c("ENSG000001", "ENSG000001"),
  padj = c(0.01, 0.01),
  delta_psi = c(0.25, -0.25)
)
obj <- add_splice_part(obj, res = res)
print(as_dt_from_s4(obj, "di_events"))
```

`add_user_features` *Standardize user-supplied protein feature annotations*

Description

Internal helper that converts a user-provided feature table into the standardized long-format schema used throughout SpliceImpactR. Ensures consistent column names, data types, and coordinate logic.

Usage

```
add_user_features(x, default_database = "user")
```

Arguments

x
: A data.frame or data.table supplied by the user containing at least name, start, and stop, and optionally one or both of ensembl_transcript_id or ensembl_peptide_id.

default_database
: Character scalar giving the default value for the database column when none is provided (default "user").

Details

The function verifies the presence of required coordinate columns and at least one Ensembl identifier, fills in any missing optional columns with default values, coerces all types to their expected formats, removes invalid coordinates (stop < start), and reorders columns into the canonical schema used by [to_long_features()].

Value

A data.table with standardized columns: ensembl_transcript_id, ensembl_peptide_id, database, feature_id, name, alt_name, start, stop, and method = "manual".

---

as_dt_from_s4 *Convert S4 slots back to data.table*

Description

Convert S4 slots back to data.table

Usage

```
as_dt_from_s4(
  x,
  slot = c("raw_events", "di_events", "res_di", "matched", "sample_frame",
    "hits_sequences", "paired_hits"),
  keep_internal_keys = FALSE
)
```

Arguments

x
: ‘SpliceImpactResult‘

slot
: One of ‘raw_events‘, ‘di_events‘, ‘res_di‘, ‘matched‘, ‘sample_frame‘, ‘paired_hits‘. For backward compatibility, ‘"hits_sequences"‘ is treated as ‘"matched"‘.

keep_internal_keys
: Keep internal key columns (‘raw_key‘, ‘di_key‘, ‘pair_key‘).

Value

‘data.table‘

Examples

```
res <- data.table::data.table(
  event_id = c("E1", "E1"),
  form = c("inc", "exc"),
  inc = c("100-110", "120-130"),
  exc = c("120-130", "100-110"),
  chr = c("chr1", "chr1"),
  strand = c("+", "+"),
  gene_id = c("ENSG000001", "ENSG000001"),
  padj = c(0.01, 0.01),
  delta_psi = c(0.20, -0.20)
)
obj <- as_splice_impact_result(res = res)
print(as_dt_from_s4(obj, "di_events"))
```

---

as_granges_hits — *Convert paired hits to GRanges*

Description

Convert paired hits to GRanges

Usage

```
as_granges_hits(hits_dt)
```

---

as_granges_res — *Convert differential table to GRanges*

Description

Convert differential table to GRanges

Usage

```
as_granges_res(res_dt)
```

---

as_segments_grl — *Convert paired hit segments to GRangesList*

Description

Convert paired hit segments to GRangesList

Usage

```
as_segments_grl(hits_dt)
```

as_se_raw_events — *Convert sample-level table to SummarizedExperiment*

Description

Convert sample-level table to SummarizedExperiment

Usage

```
as_se_raw_events(data_dt)
```

as_splice_impact_result — *Build S4 SpliceImpact container*

Description

Accepts any subset of ‘data‘, ‘res‘, and ‘hits_final‘. Missing pieces are stored as empty valid slots and can be added later with [add_splice_part()].

Usage

```
as_splice_impact_result(
  data = NULL,
  res = NULL,
  res_di = NULL,
  matched = NULL,
  sample_frame = NULL,
  hits_final = NULL,
  metadata = list()
)
```

Arguments

data	Optional sample-level input table.
res	Optional differential inclusion result table.
res_di	Optional threshold-filtered differential inclusion table.
matched	Optional annotation-matched DI table.
sample_frame	Optional sample manifest table.
hits_final	Optional paired/final hit table.
metadata	Optional list.

Value

'SpliceImpactResult'

Examples

```
raw <- data.table::data.table(
  event_id = c("E1", "E1"),
  form = c("inc", "exc"),
  sample = c("S1", "S1"),
  chr = c("chr1", "chr1"),
  strand = c("+", "+"),
  inc = c("100-110", "120-130"),
  exc = c("120-130", "100-110"),
  psi = c(0.70, 0.30),
  inclusion_reads = c(70, 30),
  exclusion_reads = c(30, 70)
)
res <- data.table::data.table(
  event_id = c("E1", "E1"),
  form = c("inc", "exc"),
  inc = c("100-110", "120-130"),
  exc = c("120-130", "100-110"),
  chr = c("chr1", "chr1"),
  strand = c("+", "+"),
  gene_id = c("ENSG000001", "ENSG000001"),
  padj = c(0.01, 0.01),
  delta_psi = c(0.20, -0.20)
)
hits <- data.table::data.table(
  event_id = "E1",
  event_type = "SE",
  gene_id = "ENSG000001",
  chr = "chr1",
  strand = "+",
  transcript_id_control = "TX1",
  transcript_id_case = "TX2",
  inc_control = "100-110",
  inc_case = "100-115",
  exc_control = "120-130",
  exc_case = "121-130",
  n_ppi = 1L,
  diff_n = 1L
)
obj <- as_splice_impact_result(data = raw, res = res, hits_final = hits)
obj
```

`attach_sequences` *Attach transcript and protein sequences to an event or annotation table*

Description

Merges sequence data (transcript and protein sequences) onto an input table of splicing events or transcript annotations, by matching on `transcript_id`. When multiple sequences share the same `transcript_id`, the function keeps the entry with a non-missing `protein_id` and the longest `protein_seq`.

Usage

```
attach_sequences(x, sequences, return_class = c("auto", "data.table", "S4"))
```

Arguments

`x`	A data.frame or data.table containing a `transcript_id` column.
`sequences`	A data.frame or data.table with at least the columns: `transcript_id`, `protein_id`, `transcript_seq`, and `protein_seq`.
`return_class`	Character. Output mode: ‘"data.table"‘, ‘"S4"‘, or ‘"auto"‘ (default). In ‘auto‘, S4 input returns updated S4 output.

Details

The join is left-sided: all rows from `x` are preserved. Duplicate `transcript_id`s in `sequences` are resolved internally based on protein presence and sequence length.

Value

A data.table with the same rows as `x` and appended sequence columns (`transcript_seq`, `protein_seq`, etc.).

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annots <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annots$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annots$sequences)
print(x_seq)
```

`attr_get` *Extract an attribute value from GTF/GFF attribute fields (internal)*

Description

Parses a specific key-value pair from the ‘attributes‘ column of a GTF/GFF line, returning the value associated with the requested key.

Usage

```
attr_get(x, key, strip = FALSE)
```

Arguments

x	Character vector of attribute strings.
key	Character string naming the attribute key to extract (e.g., ‘"gene_id"‘ or ‘"transcript_id"‘).
strip	Logical; if ‘TRUE‘, removes version suffixes using [strip_ver()].

Value

Character vector of extracted values, ‘NA‘ where the key was not found.

`bin_under_cap` *Bin elements under a cumulative cap (internal)*

Description

Internal helper that groups elements sequentially into bins such that the cumulative value in each bin does not exceed a specified cap. Often used to split items for batch processing or job chunking based on approximate size or cost.

Usage

```
bin_under_cap(df, name_col, value_col, cap = 3100)
```

Arguments

df	A `data.frame` containing at least two columns: one with element names and one with numeric values.
name_col	Character string giving the column name for element identifiers.
value_col	Character string giving the column name for numeric values used in cumulative binning.
cap	Numeric scalar giving the maximum cumulative value allowed per bin (default `3100`).

Details

The function walks through rows in order, adding elements to the current bin until the running total exceeds `cap`, then starts a new bin. The algorithm is greedy: it does not reorder or rebalance after bin formation.

Value

A list where each element is a character vector of names that belong to one bin. The bins are created sequentially in the order of the input rows.

`build_domain_lookup` *Internal helper that constructs per-exon (‘Dexon‘) and per-transcript (‘Dtx‘) mappings of domain identifiers from an exon-feature annotation table.*

Description

Internal helper that constructs per-exon (‘Dexon‘) and per-transcript (‘Dtx‘) mappings of domain identifiers from an exon-feature annotation table.

Usage

```
build_domain_lookup(exon_features)
```

Arguments

`exon_features`	‘data.frame‘ containing exon-feature relationships with amino acid start/end positions.

Value

A named ‘list‘ with:

‘Dexon‘ ‘data.table‘ keyed by ‘transcript_id, exon_id‘

‘Dtx‘ ‘data.table‘ keyed by ‘transcript_id‘

`build_from_annotations` *Build exon and transcript tables from a parsed annotation*

Description

Constructs standardized exon and transcript data tables from a flattened annotation object such as one produced by [rtracklayer::import()] on a GTF file.

Usage

```
build_from_annotations(ann)
```

Arguments

`ann`	A ‘data.frame‘ or ‘data.table‘ containing parsed gene annotation records with at least the following columns: `type`, `chr`, `start`, `end`, `strand`, `gene_id`, `gene_name`, `transcript_id`, `transcript_name`, `transcript_type`, `protein_id`, `exon_id`, and `exon_number`.

Details

This function is used internally to prepare lightweight annotation summaries for downstream event mapping and HIT-index aggregation. It does not query external resources and assumes the input annotation already includes both exon and transcript entries.

Value

A named list with three components:

‘exons‘ A ‘data.table‘ of exon records with added ‘classification‘ (‘"first"‘, ‘"last"‘, or ‘"internal"‘) determined per transcript.

‘transcripts‘ A ‘data.table‘ of transcript records.

‘protein_tx‘ Character vector of transcript IDs annotated as protein-coding (non-NA ‘protein_id‘).

---

coerce_to_dt *Coerce input to data.table for internal pipelines*

Description

Coerce input to data.table for internal pipelines

Usage

```
coerce_to_dt(
  x,
  what = c("raw_events", "di_events", "res_di", "matched", "sample_frame",
    "hits_sequences", "paired_hits")
)
```

---

collapse_domains *Internal helper that collapses a character vector of domain identifiers into a single, stable | delimited string.*

Description

Internal helper that collapses a character vector of domain identifiers into a single, stable | delimited string.

Usage

```
collapse_domains(v)
```

Arguments

v	Character vector of domain identifiers.

Value

Single string joining unique sorted identifiers.

---

compare_frames *Identify frameshifts and rescue events between transcript pairs*

Description

Function that evaluates whether inclusion and exclusion transcript isoforms for each alternative splicing event maintain the reading frame or induce a frameshift. Optionally identifies "rescue" cases where downstream coding structure re-aligns the frame.

Usage

```
compare_frames(hits, annotations, allow_ale_fs = FALSE)
```

Arguments

hits	‘data.frame‘ or ‘data.table‘ containing splicing event metadata, typically output from [compare_sequences_alignment()]. Must include columns such as ‘event_type‘, ‘transcript_id_case‘, ‘transcript_id_control‘, ‘exons_case‘, ‘exons_control‘, and ‘pc_class‘.
annotations	from get_annotations (annotations)
allow_ale_fs	Logical (default ‘FALSE‘). Whether to allow ALE/HLE events to be considered frameshifting.

Value

A ‘data.table‘ identical to ‘hits‘ with four appended columns:

frame_call ‘"FrameShift"‘ or ‘"PartialMatch"‘.

rescue Rescue classification (e.g. ‘"noRescue"‘ or type string).

frame_check_exon1 Exon ID used for inclusion isoform comparison.

frame_check_exon2 Exon ID used for exclusion isoform comparison.

See Also

[build_coding_index()], [.compare_boundary_start()], [.compare_boundary_end()], [.compare_at_overlap_start()], [.compare_at_overlap_end()], [.compare_overlap_frames()], [.find_rescue()], [.incoming_upstream_shift()], [.needs_upstream_check()]

`compare_hit_index` *Compare HIT index values between conditions*

Description

Computes per-event differences in the **HIT index** (Hybrid Intron Tolerance) between control and test conditions, performs t test, adjusts for multiple testing, and produces summary visualizations.

Usage

```
compare_hit_index(
  sample_df,
  condition_map = c(control = "control", test = "case"),
  minimum_proportion = 0.5,
  top_n_heatmap = 5000,
  sig_delta = 0.2,
  fdr_thresh = 0.05
)
```

Arguments

`sample_df`	‘data.frame‘ or ‘data.table‘ containing sample metadata with columns: ‘path‘, ‘sample_name‘, and ‘condition‘.
`condition_map`	Named character vector mapping experimental groups, e.g. ‘c(control = "control", test = "case")‘.
`minimum_proportion`	Minimum proportion of samples per group that must have valid HIT values for a test to be performed (default = 0.5).
`top_n_heatmap`	Integer; number of events to display in the heatmap ordered by absolute deltaHIT (default = 5000).
`sig_delta`	Absolute deltaHIT threshold for volcano highlighting (default = 0.2).
`fdr_thresh`	FDR threshold for volcano significance lines (default = 0.05).

Details

For each exon-level HIT index event:

- Computes mean HIT per group (‘control‘, ‘test‘)
- Performs a t test if both groups have >50
- Adjusts p-values via Benjamini-Hochberg FDR
- Computes signed (‘diff_HIT‘) and absolute (‘delta_HIT‘) changes

The function returns both the full per-event results table and a combined 2x2 patchwork plot containing:

1. Control vs Test mean HIT scatter
2. Top |deltaHIT| heatmap (control/test columns)
3. Volcano plot of |deltaHIT| vs -log10(FDR)
4. Density of deltaHIT distribution

Value

A named list with:

'results' Data.table of per-event statistics (means, p, FDR, deltaHIT)

'plot' Patchwork object with 4-panel summary visualization

See Also

[.getHITindex()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_compare <- compare_hit_index(sample_frame, condition_map = c(control = "control", test = "case"))
print(hit_compare)
```

---

compare_sequences_alignment

Compare isoform nucleotide and protein sequences by pairwise alignment

---

Description

Performs transcript- and protein-level global alignments between included and excluded isoform sequences to quantify sequence similarity, coding differences, and exon coverage differences.

Usage

```
compare_sequences_alignment(
  hits,
  annotations,
  include_sequences = FALSE,
  verbose = TRUE
)
```

Arguments

hits
: A data.table or data.frame containing isoform pairs. Must include columns: `transcript_seq_case`, `transcript_seq_control`, `protein_seq_case`, and `protein_seq_control`. From prior analysis.

annotations
: output from get_annotations (annotations)

include_sequences
: Logical; if `TRUE`, retains raw sequences in the output. Defaults to `FALSE`.

verbose
: Logical; if `TRUE`, prints processing messages.

Details

This function wraps internal helpers for alignment (`.align_dna()`, `.align_aa()`), exon length summarization (`.sum_exon_lengths()`), and protein-coding classification (`.pc_class()`).

Value

A data.table with added columns describing sequence length, coding length, and alignment similarity metrics, including:

- `pc_class`: protein-coding status ("protein_coding", "onePC", "noPC")
- `prot_len_case/control`: protein sequence lengths
- `tx_len_case/control`: transcript sequence lengths
- `exon_cds_len_*`, `exon_len_*`: summed exon/CDS lengths
- `dna_pid`, `dna_score`, `prot_pid`, `prot_score`: alignment metrics

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annots <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annots$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annots$sequences)
pairs <- get_pairs(x_seq, source="multi")
aligned <- compare_sequences_alignment(pairs, annots$annotations)
print(aligned)
```

compare_sequence_frame

Compare frame states after sequence alignment

Description

Wrapper function that performs sequence alignment (via [compare_sequences_alignment()]) and frame-shift analysis (via [compare_frames()]) for a complete set of inclusion/exclusion transcript pairs. It then summarizes each event by a high-level classification label.

Usage

```
compare_sequence_frame(
  complete_hits,
  ann,
  return_class = c("auto", "data.table", "S4")
)
```

Arguments

`complete_hits`	‘data.frame‘, ‘data.table‘, or ‘SpliceImpactResult‘ containing complete event information for inclusion/exclusion transcript pairs, typically from [get_pairs()] or similar.
`ann`	Annotation object (output of [get_annotation()]) used for both sequence alignment and coding index construction.
`return_class`	Character. Output mode: ‘"data.table"‘, ‘"S4"‘, or ‘"auto"‘ (default). In ‘auto‘, S4 input returns updated S4 output.

Details

‘compare_sequence_frame()‘ is a convenience function that integrates sequence and frame comparison stages in one call, producing an annotated table suitable for downstream summarization or visualization.

The summary label ‘summary_classification‘ follows this precedence: 1. ‘"Match"‘ - identical protein sequences. 2. ‘"FrameShift"‘ - frame disrupted. 3. ‘"Rescue"‘ - frame restored downstream. 4. Otherwise, inherited from ‘pc_class‘.

Value

A ‘data.table‘ (or updated ‘SpliceImpactResult‘ when ‘return_class‘ resolves to S4) containing all columns from ‘complete_hits‘, plus:

frame_call Result from [compare_frames()].

rescue Rescue classification.

summary_classification One of ‘"FrameShift"‘, ‘"Rescue"‘, ‘"Match"‘, or the original ‘pc_class‘.

See Also

[compare_frames()], [compare_sequences_alignment()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annots <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annots$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annots$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annots$annotations)
print(seq_compare)
```

---

compare_transcript_pairs

Compare user-selected transcript pairs

Description

Builds a matched-like table for pairs of transcripts by extracting all coding exon coordinates from annotations.

Usage

```
compare_transcript_pairs(transcript_pairs, annotations)
```

Arguments

`transcript_pairs`
: data.frame with columns ‘transcript1‘, ‘transcript2‘

`annotations`
: flattened GTF-style data.frame or data.table (from get_annotation)

Value

data.table mimicking ‘matched‘ structure, ready for downstream comparison.

Examples

```
annotation_df <- load_example_data("annotation_df")$annotation_df
pairs <- data.frame(
    transcript1 = c("ENST00000337907", "ENST00000426559"),
    transcript2 = c("ENST00000400908", "ENST00000399728")
)
matched <- compare_transcript_pairs(pairs, annotation_df$annotations)
print(matched)
```

cutoff_num — *Compute Cook's Distance Threshold*

Description

Converts a Cook's distance cutoff specification into a numeric threshold. Used internally by ['.site_glm()'] and [fit_sites_parallel()].

Usage

```
cutoff_num(n_rows, cooks_cutoff)
```

Arguments

n_rows	Integer. Number of observations in the model.
cooks_cutoff	Character or numeric. One of: **"Inf"** No filtering. **"4/n"** Use the rule-of-thumb 4 / n threshold. **numeric** Explicit numeric value.

Value

Numeric scalar cutoff value.

domains_on_exons — *Internal helper that returns all domain identifiers overlapping a given set of exons within a transcript.*

Description

Internal helper that returns all domain identifiers overlapping a given set of exons within a transcript.

Usage

```
domains_on_exons(Dexon, tx, exons_vec)
```

Arguments

Dexon	Output of [build_domain_lookup()] ('Dexon' element).
tx	Character scalar; transcript ID.
exons_vec	Character vector of exon IDs.

Value

Character vector of unique domain identifiers for those exons.

domains_on_protein — *Internal helper returning all domains mapped to a given transcript's protein.*

Description

Internal helper returning all domains mapped to a given transcript's protein.

Usage

```
domains_on_protein(Dtx, tx)
```

Arguments

Dtx	Output of [build_domain_lookup()] (‘Dtx‘ element).
tx	Character scalar; transcript ID.

Value

Character vector of domain identifiers.

enrich_by_db — *Run domain enrichment by database*

Description

Convenience wrapper for [enrich_domains_hypergeo()] that runs the enrichment test separately for each database (e.g. ‘"Pfam"‘, ‘"SMART"‘) and combines the results.

Usage

```
enrich_by_db(hits, background, dbs, ...)
```

Arguments

hits, background	See [enrich_domains_hypergeo()].
dbs	Character vector of database prefixes to test.
...	Additional arguments passed to [enrich_domains_hypergeo()].

Value

Combined ‘data.table‘ with an added ‘database‘ column.

See Also

[enrich_by_event()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)

bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)

enriched_domains <- enrich_by_db(hits_domain, bg, dbs = 'interpro')
print(enriched_domains)
```

---

enrich_by_event *Run domain enrichment by event type*

Description

Convenience wrapper for [enrich_domains_hypergeo()] that runs the enrichment test separately for each event type and combines results.

Usage

```
enrich_by_event(hits, background, events, ...)
```

Arguments

hits, background	See [enrich_domains_hypergeo()].
events	Character vector of event types to analyze.
...	Additional arguments passed to [enrich_domains_hypergeo()].

Value

Combined ‘data.table‘ with an added ‘event_type‘ column.

See Also

[enrich_by_db()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)

bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)

enriched_domains <- enrich_by_event(hits_domain, bg, events = 'AFE', db_filter = 'interpro')
print(enriched_domains)
```

---

enrich_domains_hypergeo

Domain-level enrichment via hypergeometric test

Description

Tests whether particular protein domains are overrepresented among inclusion/exclusion transcript pairs (foreground) relative to a matched background set, using the hypergeometric test.

Usage

```
enrich_domains_hypergeo(
  hits,
  background,
  domain_col_fg = "either_domains_list",
  domain_col_bg = "total_sd_domains",
  event_col = "event_type",
  event_filter = NULL,
  db_filter = NULL,
  min_fg_count = 2,
  delim = "[,;|[:space:]]+"
)
```

Arguments

`hits`	‘data.frame‘ or ‘data.table‘ containing the foreground transcript pairs (typically the significant inclusion/exclusion events). Must include a list column of domain IDs (default: ‘"either_domains_list"‘).
`background`	‘data.frame‘ or ‘data.table‘ representing the matched background pairs. Must include a list column of domain IDs (default: ‘"total_sd_domains"‘).
`domain_col_fg`	Name of the domain list column in ‘hits‘.
`domain_col_bg`	Name of the domain list column in ‘background‘.
`event_col`	Name of the column giving event type (default: ‘"event_type"‘). Set ‘NULL‘ to skip event filtering.
`event_filter`	Character vector of event types to include (e.g. ‘"A5SS"‘, ‘"A3SS"‘). If ‘NULL‘, all events are used.
`db_filter`	Character vector of database prefixes to retain (e.g. ‘"Pfam"‘, ‘"SMART"‘). If ‘NULL‘, all domains are used.
`min_fg_count`	Minimum number of foreground hits required to test a domain (default ‘2‘).
`delim`	Regular expression describing the delimiters in string list columns (default ‘[,;|[:space:]]+‘).

Details

Each domain identifier is counted once per transcript pair based on its presence in a list column (e.g. ‘either_domains_list‘). The probability of observing at least ‘k‘ such pairs is computed under the hypergeometric distribution

$$P(X \geq k), \quad X \sim \text{Hypergeom}(M, B - M, K)$$

where:

- `K` = number of foreground pairs,
- `B` = number of background pairs,
- `M` = background count of pairs containing the domain,
- `k` = foreground count of pairs containing the domain.

P-values are Benjamini-Hochberg adjusted (‘padj‘).

Optionally, analyses can be restricted by event type or database prefix (e.g. ‘"Pfam"‘, ‘"SMART"‘) and domains with fewer than ‘min_fg_count‘ foreground occurrences are skipped.

Value

A ‘data.table‘ with one row per domain, including:

‘domain_id‘ Domain identifier (database prefix removed).

‘db‘ Database prefix (e.g. ‘"Pfam"‘).

‘k‘, ‘K‘ Foreground domain count and total foreground pairs.

‘M‘, ‘B‘ Background domain count and total background pairs.

‘fg_prop‘, ‘bg_prop‘ Proportion of pairs with the domain.

‘OR‘ Odds ratio (Haldane-Anscombe corrected).

‘pval‘, ‘padj‘ Raw and BH-adjusted p-values.

‘events‘ Event IDs contributing to the domain count.

See Also

* [enrich_by_event()] run per event type * [enrich_by_db()] run per database * [add_domain_columns()] attach domain lists to hits

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)

bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)

enriched_domains <- enrich_domains_hypergeo(hits_domain, bg, db_filter = 'interpro')
print(enriched_domains)
```

`explode_coords` *Expand semicolon-delimited coordinate strings into long-format tables*

Description

Parses inclusion or exclusion coordinate strings of the form ‘"start-end;start-end;..."‘ into per-exon start/stop rows.

Usage

```
explode_coords(ev, which = c("inc", "exc"))
```

Arguments

`ev`	A ‘data.frame‘ or ‘data.table‘ containing at least ‘inc‘, ‘exc‘, ‘event_type‘, ‘gene_id‘, ‘chr‘, ‘strand‘, and ‘form‘ columns.
`which`	Character. One of ‘"inc"‘ or ‘"exc"‘ specifying which coordinate column to explode (default ‘"inc"‘).

Details

This helper is used internally to vectorize exon coordinate parsing for downstream construction of ‘GRanges‘ or other genomic features.

Value

A ‘data.table‘ with one row per coordinate interval containing: ‘event_row‘, ‘event_type‘, ‘gene_id‘, ‘chr‘, ‘strand‘, ‘form‘, ‘event_id‘, ‘start‘, ‘stop‘, and optionally ‘inc_idx‘ (ordinal index for inclusion parts).

`filter_spliceimpact_hits` *Filter a SpliceImpactResult by arbitrary paired-hit columns*

Description

Filters ‘paired_hits‘ using one or more logical expressions evaluated in the paired-hit table, then synchronizes all event-linked slots (‘segments‘, ‘res_di‘, ‘di_events‘, ‘matched‘, ‘raw_events‘).

Usage

```
filter_spliceimpact_hits(obj, ..., keep_sample_frame = TRUE)
```

Arguments

obj
: A [SpliceImpactResult].

...
: Logical filter expressions evaluated in paired-hit context (e.g., ‘event_id == "A3SS:44"‘, ‘n_ppi > 0‘, ‘frame_call == "Match"‘). Multiple expressions are combined with ‘&‘.

keep_sample_frame
: Logical; keep ‘sample_frame‘ unchanged (default ‘TRUE‘).

Value

Filtered [SpliceImpactResult].

Examples

```
hits <- data.table::data.table(
  event_id = c("E1", "E2"),
  event_type = c("SE", "A3SS"),
  gene_id = c("ENSG000001", "ENSG000002"),
  chr = c("chr1", "chr2"),
  strand = c("+", "-"),
  transcript_id_control = c("TX1", "TX3"),
  transcript_id_case = c("TX2", "TX4"),
  inc_control = c("100-110", "200-210"),
  inc_case = c("100-115", "205-215"),
  exc_control = c("120-130", "220-230"),
  exc_case = c("121-130", "225-235"),
  n_ppi = c(1L, 0L),
  diff_n = c(1L, 0L),
  frame_call = c("Match", "Frameshift")
)
obj <- as_splice_impact_result(hits_final = hits)
obj_keep <- filter_spliceimpact_hits(obj, n_ppi > 0L)
print(as_dt_from_s4(obj_keep, "paired_hits"))
```

---

fit_sites_parallel *Parallel Quasi-binomial GLM Fitting Across Sites*

Description

Fits quasi-binomial GLMs per splicing site (or event) in parallel, splitting data into chunks to limit overhead. Each site-level fit is performed by [‘.site_glm()‘].

Usage

```
fit_sites_parallel(
  x,
  chunk_size = 2000L,
  progress = TRUE,
```

```
  verbose = TRUE,
  cooks_cutoff,
  BPPARAM = BiocParallel::SerialParam()
)
```

Arguments

`x`	A ‘data.frame‘ or ‘data.table‘ with columns: ‘site_id‘, ‘condition‘, ‘psi_adj‘, ‘psi_raw‘, and ‘total‘.
`chunk_size`	Integer. Approximate number of sites per chunk to send to each worker (default 2000).
`progress`	Logical. Show progress bar (default ‘TRUE‘).
`verbose`	Logical. Print progress messages (default ‘TRUE‘).
`cooks_cutoff`	Numeric or character. Cook’s distance cutoff, passed to [cutoff_num()].
`BPPARAM`	A [BiocParallel::BiocParallelParam-class] object controlling backend and worker settings. Default is [BiocParallel::SerialParam()].

Value

A ‘data.table‘ with one row per site and columns: ‘site_id‘, ‘p.value‘, ‘cooks_max‘, ‘n‘, ‘n_used‘, ‘mean_psi_ctrl‘, ‘mean_psi_case‘, and ‘delta_psi‘.

`getSizeFactors` *Compute library size factors from exon-level read counts*

Description

Estimates per-sample normalization factors (size factors) using the **median-of-ratios** method based on exon-level read coverage (nUP + nDOWN). This approach provides robust depth normalization for splicing event comparisons.

Usage

```
getSizeFactors(df)
```

Arguments

`df`	‘data.frame‘ or ‘data.table‘ with at least columns: ‘sample_name‘, ‘exon‘, ‘nUP‘, ‘nDOWN‘.

Details

The function aggregates reads per exon across samples, constructs an exon x sample matrix, and computes size factors:

$$SF_j = median_i((counts_{ij} + 1)/geoMean_i)$$

where the geometric mean is computed across samples for each exon.

Value

A ‘data.frame‘ identical to the input with an added ‘sizeFactor‘ column, suitable for downstream normalization.

See Also

[.get_size_factors_from_exons()]

`get_annotation` *Load and cache GENCODE annotations, sequences, and hybrid exon annotations*

Description

This function loads GENCODE gene models (GTF), processes exon annotations, extracts transcript and protein sequences, identifies hybrid exons, and optionally caches the processed objects for future fast access.

Usage

```
get_annotation(
  load = c("link", "path", "cached", "test"),
  base_dir = NULL,
  species = c("human", "mouse"),
  release = 45,
  gtf_path = NULL,
  transcript_path = NULL,
  translation_path = NULL,
  filter_tsl = c("1", "2", "3")
)
```

Arguments

`load`	Character string specifying load mode: one of ‘"link"‘, ‘"path"‘, ‘"cached"‘, ‘"test"‘.
`base_dir`	Optional cache root. If ‘NULL‘ (default), uses a persistent package cache under ‘tools::R_user_dir("SpliceImpactR", "cache")‘. A package-specific ‘BiocFileCache‘ is created under this root.
`species`	Species label used in filenames (default ‘"human"‘).
`release`	GENCODE release version (default ‘45‘).
`gtf_path`	Path to a GTF file when ‘load = "path"‘.
`transcript_path`	Path to transcript FASTA (.fa/.fa.gz) when ‘load = "path"‘.
`translation_path`	Path to protein FASTA (.fa/.fa.gz) when ‘load = "path"‘.
`filter_tsl`	Transcript support levels to retain (default ‘c("1","2","3")‘). Transcripts outside this set are dropped unless the row is a gene record.

Details

Four loading modes are supported:

'test' Load small internal test data shipped with the package.

'cached' Load previously processed objects from package 'BiocFileCache'.

'path' Read local GTF and FASTA files, process, then cache processed objects in package 'BiocFileCache'.

'link' Download GENCODE files from URLs, process, then cache processed objects in package 'BiocFileCache'. Optional 'gtf_path', 'transcript_path', and 'translation_path' are only used as overrides when they are existing local files or valid URLs; otherwise downloaded GENCODE assets are used.

Processed objects are cached in package 'BiocFileCache' entries:

```
annotation/{species}/v{release}/tsl-{...}/annotations.rds
annotation/{species}/v{release}/tsl-{...}/sequences.rds
annotation/{species}/v{release}/tsl-{...}/hybrids.rds
```

Value

A list with:

'annotations' Processed long-format GTF as 'data.table'

'sequences' List with elements 'transcripts' and 'proteins' (or 'NULL' if not loaded)

'hybrids' Hybrid exon annotation list

Examples

```
# Load bundled test data
ann <- load_example_data("annotation_df")$annotation_df
print(ann)

# Load from local files and cache processed objects
# ann <- get_annotation(
#   load = "path",
#   gtf_path = "/downloaded_gtf_directory/gencode.v45.annotation.gtf.gz",
#   transcript_path = "/downloaded_gtf_directory/gencode.v45.pc_transcripts.fa.gz",
#   translation_path = "/downloaded_gtf_directory/gencode.v45.pc_translations.fa.gz"
# )

# Download files, process, and cache to a custom cache root
# ann <- get_annotation(
#   load = "link",
#   base_dir = "/project/annotation_cache/"
# )

# Load from cached RDS (fast)
# ann <- get_annotation(
#   load = "cached",
#   base_dir = "/project/annotation_cache/"
```

```
# )
```

---

get_background — *Build a transcript-pair background with domain and length annotations*

Description

Constructs a background dataset of transcript pairs suitable for domain-level or exon-level enrichment analyses. Depending on the `source` parameter, the function can derive the background from HIT index results, annotated transcripts, or a user-provided list of transcript IDs.

Usage

```
get_background(
  source = c("hit_index", "annotated", "user-given"),
  input,
  annotations,
  protein_features,
  keep_annotated_first_last = TRUE,
  minOverlap = 0.8,
  BPPARAM = BiocParallel::bpparam()
)
```

Arguments

`source`
: Character string specifying the source of the background. One of:
  - `"hit_index"` use HIT index output directories.
  - `"annotated"` use all transcripts from the annotation.
  - `"user-given"` use a user-supplied list of transcript IDs.

`input`
: Source-specific input:
  - For `"hit_index"`: a data.frame of paths with a `path` column.
  - For `"annotated"`: ignored.
  - For `"user-given"`: a character vector or data.frame containing `transcript_id`.

`annotations`
: A data.table annotations from `get_annotations`

`protein_features`
: A data.frame of protein domain or motif features (e.g. InterPro, Pfam) with at least `ensembl_transcript_id`, `ensembl_peptide_id`, `database`, and `name` columns from `get_comprehensive_annotations`

`keep_annotated_first_last`
: Logical; passed to read_background to control filtering of annotated first/last exons. Defaults to `TRUE`.

`minOverlap`
: Numeric (0-1); minimum fraction overlap required when matching exons between HIT index data and annotations. Defaults to 0.8.

`BPPARAM`
: A [BiocParallel::BiocParallelParam-class] object controlling parallel execution in domain background calculations. Defaults to [BiocParallel::bpparam()].

Value

A data.table in which each row represents a transcript pair annotated with gene ID, CDS/exon length differences, and protein domain differences. Columns include: `gene_id`, `transcript_id_1`, `transcript_id_2`, `prot_aa_1`, `prot_aa_2`, `domains_1`, `domains_2`, and related summary metrics.

Examples

```
annots <- load_example_data("annotation_df")$annotation_df
interpro_features <- get_protein_features(c("interpro"), annots$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

# Build background from HIT index paths
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annots$annotations,
                     protein_features = protein_feature_total)

# Or from user-supplied transcript IDs
tx_ids <- c("ENST00000466994","ENST00000484435")
bg_user <- get_background(source = "user-given",
                          input = tx_ids,
                          annotations = annots$annotations,
                          protein_features = protein_feature_total)
```

---

get_biomart_protein_features

Retrieve protein feature annotations from Ensembl BioMart (internal)

Description

Internal helper to query Ensembl BioMart for per-transcript protein feature annotations such as InterPro or Pfam domains. Designed for batched retrieval using [split_into_bits()] to avoid large single queries.

Usage

```
get_biomart_protein_features(
  protein_features = c("interpro"),
  gtf_df,
  max_accession_size = 3500,
  species_dataset = "hsapiens_gene_ensembl",
  release = 109,
  ensembl_mirror = NULL
)
```

Arguments

`protein_features`
: Character vector specifying which feature types to request (e.g. "interpro", "pfam").

`gtf_df`
: A `data.frame` or `data.table` containing GTF annotations; used to derive chromosome groups for batching.

`max_accession_size`
: Integer specifying the maximum total number of transcripts per query batch (default `3500`).

`species_dataset`
: Character string giving the Ensembl BioMart dataset (default "hsapiens_gene_ensembl"). For mouse, use "mmusculus_gene_ensembl".

`release`
: Release version from Ensembl associated with the GENCODE version used in [get_annotation()]. See the GENCODE human release listing to map GENCODE and Ensembl versions.

Details

The function queries the Ensembl BioMart service using **biomaRt::getBM()** with filters "chromosome_name" and "transcript_biotype", restricted to "protein_coding" transcripts. Queries are executed in chunks per chromosome group to avoid API timeouts.

Value

A `data.table` containing protein feature annotations including transcript and peptide IDs, feature start/end positions, and database-specific identifiers (e.g., InterPro accession).

---

get_comprehensive_annotations

Combine multiple sources of protein feature annotations

Description

Aggregates all available feature tables (e.g., biomaRt + manual) into a single unified long-format annotation table.

Usage

```
get_comprehensive_annotations(
  protein_feature_list,
  load_path_list = NULL,
  save_path = NULL
)
```

Arguments

protein_feature_list
: List of `data.table` objects, typically from [get_protein_features()] or [get_manual_features()].

load_path_list
: Optional vector of file paths to load each feature source from disk (instead of providing in memory).

save_path
: Optional path to cache the combined annotations.

Value

A combined `data.table` containing all unique feature rows.

Examples

```
annotation_df <- load_example_data("annotation_df")$annotation_df
user_df <- data.frame(
  ensembl_transcript_id = c(
    "ENST00000511072","ENST00000374900","ENST00000373020","ENST00000456328",
    "ENST00000367770","ENST00000331789","ENST00000335137","ENST00000361567",
    NA,                    "ENST00000380152"
  ),
  ensembl_peptide_id = c(
    "ENSP00000426975", NA,                    "ENSP00000362048","ENSP00000407743",
    "ENSP00000356802","ENSP00000326734", NA,                  "ENSP00000354587",
    "ENSP00000364035", NA
  ),
  name = c(
    "Low complexity","Transmembrane helix","Coiled-coil","Signal peptide",
    "Transmembrane helix","Low complexity","Coiled-coil","Transmembrane helix",
    "Signal peptide","Low complexity"
  ),
  start = c(80L, 201L, 35L, 1L, 410L, 150L, 220L, 30L, 1L, 300L),
  stop  = c(120L,223L, 80L, 20L, 430L, 190L, 260L, 55L, 24L, 360L),
 database  = c("seg","tmhmm","ncoils","signalp","tmhmm","seg","ncoils","tmhmm","signalp", NA),
 alt_name  = c(NA,"TMhelix",NA,"SignalP-noTM", "TMhelix", NA, NA, "TMhelix", "SignalP-TAT", NA),
  feature_id = c(NA, NA, NA, NA, NA, NA, NA, NA, NA, NA)
)
user_features <- get_manual_features(user_df, annotation_df$annotations)
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(user_features, interpro_features))
print(protein_feature_total)
```

---

get_differential_inclusion

Differential Inclusion Analysis from Hit Index Tables

Description

Performs per-site differential inclusion testing from a hit-index or junction-form table. Each site is modeled with a quasi-binomial GLM (‘psi_adj ~ condition‘) to estimate deltaPSI and significance, optionally using parallel processing.

Usage

```
get_differential_inclusion(
  DT,
  min_total_reads = 10L,
  minimum_proportion_containing_event = 0.5,
  terminal_fill = "event_max",
  cooks_cutoff = "Inf",
  adjust_method = "fdr",
  verbose = TRUE,
  parallel_glm = TRUE,
  chunk_size_glm = 1000,
  BPPARAM = BiocParallel::SerialParam(),
  return_class = c("auto", "data.table", "S4")
)
```

Arguments

`DT` A ‘data.frame‘, ‘data.table‘, or ‘SpliceImpactResult‘ containing at least the columns ‘event_type‘, ‘gene_id‘, ‘chr‘, ‘inc‘, ‘exclusion_reads‘, ‘inclusion_reads‘, ‘condition‘, and ‘sample‘.

`min_total_reads` Integer. Minimum total reads per site/sample required for inclusion (default ‘10‘).

`minimum_proportion_containing_event` Numeric in ‘[0,1]‘. Minimum fraction of samples per condition that must contain the event (default ‘0.5‘).

`terminal_fill` Character or numeric. Strategy for completing AFE/ALE events that are missing in a given sample. Choose one of:

- **"none"** Do not add missing terminal sites.
- **"gene_max"** Fill missing sites with zero counts and set ‘total‘ to the maximum observed within each ‘gene_id‘/‘sample‘/‘condition‘ group.
- **"event_max"** Fill missing sites with zero counts and set ‘total‘ to the maximum observed within each ‘event_id‘/‘sample‘/‘condition‘ group.
- **"zero"** Fill missing sites with zero counts and ‘total = 0‘.

Alternatively, supply a single numeric value to use as the ‘total‘ for all filled rows. Defaults to ‘"gene_max"‘.

`cooks_cutoff` Character or numeric. Cook’s distance cutoff: ‘"4/n"‘, ‘"Inf"‘, ‘"none"‘, or a numeric value.

`adjust_method` Character. Multiple-testing correction method passed to [stats::p.adjust()] (default ‘"fdr"‘).

verbose	Logical. Print progress messages (default ‘TRUE‘).
parallel_glm	Logical. Use parallel fitting via [fit_sites_parallel()] (default ‘TRUE‘).
chunk_size_glm	Integer. Number of sites per parallel chunk (default ‘1000‘).
BPPARAM	A [BiocParallel::BiocParallelParam-class] object used when ‘parallel_glm = TRUE‘. Default is [BiocParallel::SerialParam()].
return_class	Character. Output mode: ‘"data.table"‘, ‘"S4"‘, or ‘"auto"‘ (default). In ‘auto‘, S4 input returns an updated S4 object; otherwise a ‘data.table‘ is returned.

Details

The function filters out low-coverage and low-presence events, optionally fills AFE/ALE sites with zero counts where necessary, and then applies site-level GLMs. Parallelization uses [BiocParallel] back-ends for reproducibility across platforms. To run in parallel, supply ‘BPPARAM‘ (for example [BiocParallel::MulticoreParam()] on Linux/macOS or [BiocParallel::SnowParam()] on Windows).

Value

If ‘return_class‘ resolves to ‘"data.table"‘, a ‘data.table‘ with one row per site containing:

- Metadata columns (‘site_id‘, ‘event_type‘, ‘event_id‘, ‘gene_id‘, ...)
- Sample counts (‘n_samples‘, ‘n_control‘, ‘n_case‘)
- Mean PSI per group (‘mean_psi_ctrl‘, ‘mean_psi_case‘)
- deltaPSI (‘delta_psi‘)
- Raw and adjusted p-values (‘p.value‘, ‘padj‘)
- Maximum Cook’s distance (‘cooks_max‘)

See Also

[fit_sites_parallel()], [cutoff_num()], [stats::glm()], [BiocParallel::bplapply()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
head(res)
```

get_di_gene_enrichment

Extract Differential-Inclusion Genes for Enrichment

Description

Select genes whose splicing passes significance and effect-size thresholds.

Usage

```
get_di_gene_enrichment(hits, padj_threshold, delta_psi_threshold)
```

Arguments

`hits`	Data frame output from differential inclusion testing.
`padj_threshold`	FDR cutoff (default '0.05').
`delta_psi_threshold`	Absolute deltaPSI threshold (default '0.1').

Value

Character vector of gene IDs.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)

annotation_df <- load_example_data("annotation_df")$annotation_df
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
hits_domain <- get_domains(seq_compare, exon_features)

bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)
enrichment <- get_enrichment(get_di_gene_enrichment(res, .05, .1), bg$gene_id, species = 'human', 'ensembl', 'MSig
print(enrichment)
```

get_domains *Add protein domain annotations to splicing events*

Description

Annotates each splicing event with protein domains that are gained, lost, or uniquely present in inclusion or exclusion isoforms.

Usage

```
get_domains(
  hits,
  exon_features,
  show_protein_domains = FALSE,
  return_class = c("auto", "data.table", "S4")
)
```

Arguments

- `hits` ‘data.frame‘, ‘data.table‘, or ‘SpliceImpactResult‘ containing transcript pairs with at least ‘transcript_id_case‘, ‘transcript_id_control‘, ‘exons_case‘, ‘exons_control‘, and ‘event_type‘.
- `exon_features` ‘data.frame‘ of exon-domain annotations with columns ‘ensembl_transcript_id‘, ‘ensembl_peptide_id‘, ‘exon_id‘, ‘database‘, ‘feature_id‘, ‘name‘, ‘overlap_aa_start‘, ‘overlap_aa_end‘.
- `show_protein_domains` Logical; if ‘TRUE‘, include full protein-level domain sets (‘domains_protein_case‘ / ‘domains_protein_control‘).
- `return_class` Character. Output mode: ‘"data.table"‘, ‘"S4"‘, or ‘"auto"‘ (default). In ‘auto‘, S4 input returns updated S4 output.

Details

Internally, this function builds a domain lookup table from an exon feature annotation (e.g. InterPro, Pfam) and extracts per-exon and per-transcript domain lists for each isoform in ‘hits‘. Differences between the inclusion (‘*_case‘) and exclusion (‘*_control‘) isoforms are then summarized as:

* ‘case_only_domains‘: domains unique to the inclusion isoform * ‘control_only_domains‘: domains unique to the exclusion isoform * ‘diff_n‘: total number of non-shared domains

If ‘show_protein_domains = TRUE‘, additional columns report full domain sets across the entire inclusion/exclusion proteins.

Value

The input ‘hits‘ table with added columns (or updated ‘SpliceImpactResult‘ when ‘return_class‘ resolves to S4):

- ‘domains_exons_case‘, ‘domains_exons_control‘ domains found on event exons
- ‘case_only_domains‘, ‘control_only_domains‘ domains unique to each isoform
- ‘case_only_domains_list‘, ‘control_only_domains_list‘, ‘either_domains_list‘ list-columns
- ‘case_only_n‘, ‘control_only_n‘, ‘diff_n‘ domain counts
- optionally, ‘domains_protein_case‘ / ‘domains_protein_control‘

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)
print(hits_domain)
```

`get_domain_gene_for_enrichment`
Extract Domain-Altering Genes for Enrichment

Description

Return genes whose inclusion/exclusion isoforms show unique protein domain gain or loss.

Usage

```
get_domain_gene_for_enrichment(hits)
```

Arguments

`hits`	Data frame with domain-annotation columns.

Value

Character vector of gene IDs.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)

bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)
enrichment <- get_enrichment(get_domain_gene_for_enrichment(hits_domain), bg$gene_id, species = 'human', 'ensembl
print(enrichment)
```

---

get_enrichment *Gene Set Enrichment for Splicing-Linked Gene Lists*

Description

Perform over-representation analysis for a foreground gene set, optionally against a background universe, using GO, MSigDB, and Reactome categories.

Usage

```
get_enrichment(
  foreground,
  background = NULL,
  species = c("human", "mouse"),
  gene_id_type = c("symbol", "ensembl"),
  sources = c("GO:BP", "GO:MF", "GO:CC", "MSigDB:H", "MSigDB:C2:CP:REACTOME"),
  min_size = 10,
  max_size = 2000,
  p_adjust_cutoff = 0.05,
  simplify_go = TRUE,
  top_n_plot = 20,
  plot_type = c("dot", "bar")
)
```

Arguments

`foreground` Character vector of gene IDs (symbols or Ensembl IDs).

`background` Optional character vector of background genes (universe). If ‘NULL‘, all genes present in annotation collections are used.

`species` Species for enrichment catalog (‘"human"‘ or ‘"mouse"‘).

`gene_id_type` Type of input gene IDs (‘"symbol"‘ or ‘"ensembl"‘).

`sources` Character vector selecting enrichment sources. Example options include:

- ‘"GO:BP"‘, ‘"GO:MF"‘, ‘"GO:CC"‘
- ‘"MSigDB:H"‘, ‘"MSigDB:C2:CP:REACTOME"‘

`min_size` Minimum term size (default ‘10‘).

`max_size` Maximum term size (default ‘2000‘).

`p_adjust_cutoff` FDR cutoff for reporting significant terms.

`simplify_go` Whether to apply GO term redundancy reduction.

`top_n_plot` Number of terms to visualize in the quick plot.

`plot_type` ‘"dot"‘ (default) or ‘"bar"‘.

Details

This is a convenience wrapper around ‘clusterProfiler‘, ‘msigdbr‘, and optionally ‘ReactomePA‘, producing a combined enrichment table and a quick visualization of top significant terms.

Input genes are internally mapped to Entrez IDs. Enrichment tests are performed using:

* ‘clusterProfiler::enrichGO‘ * ‘clusterProfiler::enricher‘ (MSigDB) * ‘ReactomePA::enrichPathway‘ (optional)

Value

A list with:

results_per_source List of enrichment result tables per source

results_combined Combined enrichment table

results_signif Filtered table by FDR cutoff

plot A ‘ggplot2‘ object visualizing top terms

Note

Requires these packages installed: ‘clusterProfiler‘, ‘msigdbr‘, ‘data.table‘, ‘AnnotationDbi‘, ‘ggplot2‘, and ‘org.Hs.eg.db‘ or ‘org.Mm.eg.db‘. For Reactome analysis you must also install ‘ReactomePA‘.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)

annotation_df <- load_example_data("annotation_df")$annotation_df
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
hits_domain <- get_domains(seq_compare, exon_features)

bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)
enrichment <- get_enrichment(res$gene_id, bg$gene_id, species = 'human', 'ensembl', 'MSigDB:H')
print(enrichment)
```

`get_example_data` *Helper to fetch test files for vignettes / tests*

Description

Helper to fetch test files for vignettes / tests

Usage

```
get_example_data(filename)
```

Arguments

`filename`	file to probe

Value

proper path to example data

get_exon_features — *Map protein features to coding exons*

Description

Overlaps amino acid-based protein features (e.g., InterPro, TMHMM) with exon coding spans defined by transcript-relative CDS coordinates.

Usage

```
get_exon_features(gtf_dt, feat, inclusive = TRUE)
```

Arguments

- `gtf_dt` — A `data.frame` or `data.table` containing transcript and exon annotation, including `type`, `transcript_id`, `cds_rel_start`, and `cds_rel_stop` columns (see [add_exon_coding_information()]).
- `feat` — A `data.frame` or `data.table` of long-format protein features (from [get_protein_features()] or [get_comprehensive_annotations()]) containing columns `ensembl_transcript_id`, `start`, `stop`, `database`, `feature_id`, `name`, and `alt_name`.
- `inclusive` — Logical; whether to round both feature and exon boundaries upward when converting from nucleotide to amino acid coordinates (default `TRUE`). If `FALSE`, downstream exons own partial codons to avoid double counting.

Value

A `data.table` of overlapping feature-exon pairs with amino acid coordinates (`overlap_aa_start`, `overlap_aa_end`, `overlap_aa_len`) and associated exon and feature metadata.

Examples

```
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)
print(exon_features)
```

get_gene_enrichment *Unified gene selector for enrichment foregrounds*

Description

Selects a foreground gene vector for enrichment from DI results (‘res‘) or hits-final-like tables (‘hits‘) using a single wrapper.

Usage

```
get_gene_enrichment(
  mode = c("di", "ppi", "domain"),
  x = NULL,
  res = NULL,
  hits = NULL,
  padj_threshold = 0.05,
  delta_psi_threshold = 0.1
)
```

Arguments

`mode`	One of ‘"di"‘, ‘"ppi"‘, ‘"domain"‘.
`x`	Optional generic input. For ‘mode="di"‘, this should be ‘res‘-like; for ‘mode="ppi"‘/‘"domain"‘, this should be hits-final-like. If ‘x‘ is S4, the appropriate slot is used automatically.
`res`	Optional DI table (or S4) used when ‘mode="di"‘. If provided, it is preferred over ‘x‘.
`hits`	Optional hits-final-like table (or S4) used when ‘mode="ppi"‘/‘"domain"‘. If provided, it is preferred over ‘x‘.
`padj_threshold`	FDR cutoff used only for ‘mode="di"‘.
`delta_psi_threshold`	Absolute delta-psi cutoff used only for ‘mode="di"‘.

Details

- ‘mode = "di"‘ uses differential inclusion columns (‘gene_id‘, ‘padj‘, ‘delta_psi‘) - ‘mode = "ppi"‘ uses hits-final-like columns (‘gene_id‘, ‘n_ppi‘) - ‘mode = "domain"‘ uses hits-final-like columns (‘gene_id‘, ‘diff_n‘)

Inputs can be a ‘data.table‘/‘data.frame‘ or a ‘SpliceImpactResult‘ S4 object.

Value

Character vector of unique gene IDs.

Examples

```
res <- data.table::data.table(
  gene_id = c("ENSG000001", "ENSG000001", "ENSG000002"),
  padj = c(0.01, 0.20, 0.03),
  delta_psi = c(0.25, 0.05, -0.30)
)
hits <- data.table::data.table(
  gene_id = c("ENSG000001", "ENSG000002", "ENSG000003"),
  n_ppi = c(1L, 0L, 2L),
  diff_n = c(0L, 1L, 2L)
)
get_gene_enrichment(mode = "di", res = res)
get_gene_enrichment(mode = "ppi", hits = hits)
get_gene_enrichment(mode = "domain", hits = hits)

hits_s4 <- data.table::data.table(
  event_id = c("E1", "E2", "E3"),
  event_type = c("SE", "A3SS", "MXE"),
  gene_id = c("ENSG000001", "ENSG000002", "ENSG000003"),
  chr = c("chr1", "chr1", "chr2"),
  strand = c("+", "+", "-"),
  transcript_id_control = c("TX1", "TX3", "TX5"),
  transcript_id_case = c("TX2", "TX4", "TX6"),
  inc_control = c("100-110", "200-210", "300-310"),
  inc_case = c("100-115", "205-215", "305-315"),
  exc_control = c("120-130", "220-230", "320-330"),
  exc_case = c("121-130", "225-235", "325-335"),
  n_ppi = c(1L, 0L, 2L),
  diff_n = c(0L, 1L, 2L)
)
obj <- as_splice_impact_result(hits_final = hits_s4)
get_gene_enrichment(mode = "ppi", x = obj)
get_gene_enrichment(mode = "domain", x = obj)
```

`get_hitindex` *Load HIT index PSI files for one or more samples/conditions.*

Description

Load HIT index PSI files for one or more samples/conditions.

Usage

```
get_hitindex(paths_df, keep_annotated_first_last = FALSE)
```

Arguments

`paths_df` Data.frame with columns: `path`, `condition`, and optionally `sample_name`.

`keep_annotated_first_last` Logical; if TRUE, retain only annotated first/last exons and normalize PSI.

Value

A standardized ‘data.table‘ of HIT index PSI values with inclusion/exclusion and metadata.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame, keep_annotated_first_last = TRUE)
print(hit_index)
```

---

get_hits_core *Convenience accessor for core paired-hit columns*

Description

Convenience accessor for core paired-hit columns

Usage

```
get_hits_core(x, drop_missing = TRUE, keep_internal_keys = FALSE)
```

Arguments

`x` A [SpliceImpactResult] object or a paired-hits ‘data.frame‘/‘data.table‘.

`drop_missing` Logical; if ‘TRUE‘, silently drops requested columns that are absent. If ‘FALSE‘, errors on missing columns.

`keep_internal_keys` Passed through when ‘x‘ is S4. Default ‘FALSE‘.

Value

‘data.table‘ with the ‘core‘ subset. Works for both S4 and paired-hits ‘data.table‘ input.

Examples

```
hits <- data.table::data.table(
  event_id = c("E1", "E2"),
  event_type = c("SE", "A3SS"),
  gene_id = c("ENSG000001", "ENSG000002"),
  chr = c("chr1", "chr2"),
  strand = c("+", "-"),
  transcript_id_control = c("TX1", "TX3"),
  transcript_id_case = c("TX2", "TX4"),
  n_ppi = c(1L, 0L),
  diff_n = c(1L, 0L)
)
print(get_hits_core(hits))
```

get_hits_domain *Convenience accessor for domain-focused paired-hit columns*

Description

Convenience accessor for domain-focused paired-hit columns

Usage

```
get_hits_domain(x, drop_missing = TRUE, keep_internal_keys = FALSE)
```

Arguments

x	A [SpliceImpactResult] object or a paired-hits ‘data.frame‘/‘data.table‘.
drop_missing	Logical; if ‘TRUE‘, silently drops requested columns that are absent. If ‘FALSE‘, errors on missing columns.
keep_internal_keys	Passed through when ‘x‘ is S4. Default ‘FALSE‘.

Value

‘data.table‘ with the ‘domain‘ subset. Works for both S4 and paired-hits ‘data.table‘ input.

Examples

```
hits <- data.table::data.table(
  event_id = c("E1", "E2"),
  event_type = c("SE", "A3SS"),
  gene_id = c("ENSG000001", "ENSG000002"),
  chr = c("chr1", "chr2"),
  strand = c("+", "-"),
  transcript_id_control = c("TX1", "TX3"),
  transcript_id_case = c("TX2", "TX4"),
  case_only_domains = c("IPR0001", ""),
  control_only_domains = c("", "IPR0002"),
  case_only_n = c(1L, 0L),
  control_only_n = c(0L, 1L),
  diff_n = c(1L, 1L)
)
print(get_hits_domain(hits))
```

get_hits_final_view *Access paired-hits as compact data.table subsets*

Description

Extracts ‘paired_hits‘ columns from a [SpliceImpactResult] (or a paired-hits ‘data.table‘) using predefined subset groups such as ‘core‘, ‘domain‘, ‘ppi‘, and ‘sequence‘.

Usage

```
get_hits_final_view(
  x,
  col_subset = c("core"),
  cols = NULL,
  drop_missing = TRUE,
  keep_internal_keys = FALSE
)
```

Arguments

x	A [SpliceImpactResult] object or a paired-hits ‘data.frame‘/‘data.table‘.
col_subset	Character vector of subset names. Any of ‘"core"‘, ‘"domain"‘, ‘"ppi"‘, ‘"sequence"‘, or ‘"all"‘.
cols	Optional explicit column vector. If supplied, ‘col_subset‘ is ignored.
drop_missing	Logical; if ‘TRUE‘, silently drops requested columns that are absent. If ‘FALSE‘, errors on missing columns.
keep_internal_keys	Passed through when ‘x‘ is S4. Default ‘FALSE‘.

Value

A ‘data.table‘ containing the selected columns. Row count and row order are preserved from the input (‘SpliceImpactResult@paired_hits‘ or provided ‘data.table‘).

Examples

```
hits <- data.table::data.table(
  event_id = c("E1", "E2"),
  event_type = c("SE", "A3SS"),
  gene_id = c("ENSG000001", "ENSG000002"),
  chr = c("chr1", "chr2"),
  strand = c("+", "-"),
  transcript_id_control = c("TX1", "TX3"),
  transcript_id_case = c("TX2", "TX4"),
  protein_id_control = c("P1", "P3"),
  protein_id_case = c("P2", "P4"),
  inc_control = c("100-110", "200-210"),
```

```
  inc_case = c("100-115", "205-215"),
  exc_control = c("120-130", "220-230"),
  exc_case = c("121-130", "225-235"),
  case_only_domains = c("IPR0001", ""),
  control_only_domains = c("", "IPR0002"),
  case_only_n = c(1L, 0L),
  control_only_n = c(0L, 1L),
  diff_n = c(1L, 1L),
  case_ppi = c("A;B", "C"),
  control_ppi = c("A", "C;D"),
  n_case_ppi = c(2L, 1L),
  n_control_ppi = c(1L, 2L),
  n_ppi = c(1L, 1L),
  dna_pid = c(0.95, 0.90),
  prot_pid = c(0.90, 0.85),
  frame_call = c("Match", "Frameshift")
)
print(get_hits_final_view(hits, col_subset = c("core", "ppi")))
```

`get_hits_ppi` *Convenience accessor for PPI-focused paired-hit columns*

Description

Convenience accessor for PPI-focused paired-hit columns

Usage

```
get_hits_ppi(x, drop_missing = TRUE, keep_internal_keys = FALSE)
```

Arguments

`x`	A [SpliceImpactResult] object or a paired-hits ‘data.frame‘/‘data.table‘.
`drop_missing`	Logical; if ‘TRUE‘, silently drops requested columns that are absent. If ‘FALSE‘, errors on missing columns.
`keep_internal_keys`	Passed through when ‘x‘ is S4. Default ‘FALSE‘.

Value

‘data.table‘ with the ‘ppi‘ subset. Works for both S4 and paired-hits ‘data.table‘ input.

Examples

```
hits <- data.table::data.table(
  event_id = c("E1", "E2"),
  event_type = c("SE", "A3SS"),
  gene_id = c("ENSG000001", "ENSG000002"),
  chr = c("chr1", "chr2"),
```

```
  strand = c("+", "-"),
  transcript_id_control = c("TX1", "TX3"),
  transcript_id_case = c("TX2", "TX4"),
  case_ppi = c("A;B", "C"),
  control_ppi = c("A", "C;D"),
  n_case_ppi = c(2L, 1L),
  n_control_ppi = c(1L, 2L),
  n_ppi = c(1L, 1L)
)
print(get_hits_ppi(hits))
```

`get_hits_sequence` *Convenience accessor for sequence/frame-focused paired-hit columns*

Description

Convenience accessor for sequence/frame-focused paired-hit columns

Usage

```
get_hits_sequence(x, drop_missing = TRUE, keep_internal_keys = FALSE)
```

Arguments

`x`	A [SpliceImpactResult] object or a paired-hits ‘data.frame‘/‘data.table‘.
`drop_missing`	Logical; if ‘TRUE‘, silently drops requested columns that are absent. If ‘FALSE‘, errors on missing columns.
`keep_internal_keys`	Passed through when ‘x‘ is S4. Default ‘FALSE‘.

Value

‘data.table‘ with the ‘sequence‘ subset. Works for both S4 and paired-hits ‘data.table‘ input.

Examples

```
hits <- data.table::data.table(
  event_id = c("E1", "E2"),
  event_type = c("SE", "A3SS"),
  gene_id = c("ENSG000001", "ENSG000002"),
  chr = c("chr1", "chr2"),
  strand = c("+", "-"),
  transcript_id_control = c("TX1", "TX3"),
  transcript_id_case = c("TX2", "TX4"),
  protein_id_control = c("P1", "P3"),
  protein_id_case = c("P2", "P4"),
  dna_pid = c(0.95, 0.90),
  prot_pid = c(0.90, 0.85),
  frame_call = c("Match", "Frameshift")
```

```
)
print(get_hits_sequence(hits))
```

`get_linear_motifs` *Get short linear motif validated instances from ELM and convert to pf form*

Description

Get short linear motif validated instances from ELM and convert to pf form

Usage

```
get_linear_motifs(
  gtf_df,
  protein_seqs,
  species = c("hsapiens_gene_ensembl", "mmusculus_gene_ensembl"),
  release = 109,
  ensembl_mirror = NULL
)
```

Arguments

`gtf_df`	A `data.frame` or `data.table` containing GTF annotations; used to derive chromosome groups for batching.
`protein_seqs`	only necessary if loading SLiMs from elm get_annotation() (default `"sequences"`) output
`species`	Character string giving the Ensembl BioMart dataset (default `"hsapiens_gene_ensembl"`). For mouse, use `"mmusculus_gene_ensembl"`.
`release`	Release version from Ensembl associated with the GENCODE version used in [get_annotation()]. See the GENCODE human release listing to map GENCODE and Ensembl versions.
`ensembl_mirror`	Optional Ensembl mirror passed to the BioMart connector.

Details

Here we access ELM's SLiM database to pull instances and classes and use BiomaRt to match up uniprot to ensembl + confirm with regex checks

Value

A `data.table` containing protein feature annotations including transcript and peptide IDs, feature start/end positions, and database-specific identifiers (e.g., InterPro accession) for elm SLiMs

get_manual_features *Incorporate user-supplied protein features*

Description

Converts a manual feature table into the standardized long format and optionally merges it with biomaRt-derived features.

Usage

```
get_manual_features(
  manual_features,
  gtf_df,
  biomaRt_features = NULL,
  load_path = NULL,
  save_path = NULL
)
```

Arguments

- `manual_features` Data.frame or data.table with at least `name`, `start`, `stop` amino acid, and one of `ensembl_transcript_id` or `ensembl_peptide_id`.
- `gtf_df` get_annotation annotation output
- `biomaRt_features` Optional `data.table` of features from [get_protein_features()] to merge with.
- `load_path` Optional path to load precomputed manual features.
- `save_path` Optional path to save the combined feature table.

Value

A `data.table` of manual (and optionally combined) protein features.

See Also

[add_user_features()]

Examples

```
annotation_df <- load_example_data("annotation_df")$annotation_df
user_df <- data.frame(
  ensembl_transcript_id = c(
    "ENST00000511072","ENST00000374900","ENST00000373020","ENST00000456328",
    "ENST00000367770","ENST00000331789","ENST00000335137","ENST00000361567",
    NA,                    "ENST00000380152"
  ),
  ensembl_peptide_id = c(
```

```
    "ENSP00000426975", NA,                   "ENSP00000362048","ENSP00000407743",
    "ENSP00000356802","ENSP00000326734", NA,                  "ENSP00000354587",
    "ENSP00000364035", NA
  ),
  name = c(
    "Low complexity","Transmembrane helix","Coiled-coil","Signal peptide",
    "Transmembrane helix","Low complexity","Coiled-coil","Transmembrane helix",
    "Signal peptide","Low complexity"
  ),
  start = c(80L, 201L, 35L, 1L, 410L, 150L, 220L, 30L, 1L, 300L),
  stop  = c(120L,223L, 80L, 20L, 430L, 190L, 260L, 55L, 24L, 360L),
 database  = c("seg","tmhmm","ncoils","signalp","tmhmm","seg","ncoils","tmhmm","signalp", NA),
 alt_name  = c(NA,"TMhelix",NA,"SignalP-noTM", "TMhelix", NA, NA, "TMhelix", "SignalP-TAT", NA),
  feature_id = c(NA, NA, NA, NA, NA, NA, NA, NA, NA, NA)
)
user_features <- get_manual_features(user_df, annotation_df$annotations)
print(user_features)
```

---

get_matched_events_chunked

Match splicing events to transcript annotations in chunks

Description

This is a wrapper around match_events_to_annotations_vec that processes large event tables in manageable chunks to reduce memory usage. It sequentially runs matching per chunk and concatenates the results.

Usage

```
get_matched_events_chunked(
  events,
  annotations,
  chunk_size = 50000,
  minOverlap = 0.05,
  return_class = c("auto", "data.table", "S4")
)
```

Arguments

`events`	A data.frame or data.table of event definitions. Must include coordinates compatible with match_events_to_annotations_vec
`annotations`	A data.frame of transcript/exon annotation rows. Typically generated by get_annotations
`chunk_size`	Integer, number of event rows to process per chunk (default = 50,000).
`minOverlap`	double ranging from 0 to 1 (default 0.05), required minimum overlap to consider a match
`return_class`	Character. Output mode: ‘"data.table"‘, ‘"S4"‘, or ‘"auto"‘ (default). In ‘auto‘, S4 input returns updated S4 output.

Details

This function is intended for large-scale event matching across many splicing events, where running the full table at once may exceed memory limits. It can later be parallelized using **future.apply** or similar.

Value

A data.table with matched transcripts and exons for all events. The output order matches the original event order.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
print(sample_frame)

hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annots <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annots$annotations, chunk_size = 2000)
print(matched)
```

---

get_pairs *Pair inclusion and exclusion forms of splicing events*

Description

Builds paired tables of inclusion/exclusion forms for splicing events from rMATS-like or HITindex-like inputs. In rMATS mode, events are paired when both INC and EXC forms exist for a given event ID. In HITindex mode, all positive and negative deltaPSI rows within each event are cross-joined.

Usage

```
get_pairs(
  x,
  source = c("paired", "multi"),
  return_class = c("auto", "data.table", "S4")
)
```

Arguments

`x`	A data.frame, data.table, or ‘SpliceImpactResult‘ containing splicing event information.
`source`	Character string specifying input structure:
	`"paired"` (rMATS-like) requires exactly one INC and one EXC per event ID.

"multi" (HITindex-like) pairs all positive and negative delta_psi values within each event.

return_class Character. Output mode: ‘"data.table"‘, ‘"S4"‘, or ‘"auto"‘ (default). In ‘auto‘, S4 input returns updated S4 output.

Details

In source="paired" mode, only events with exactly one INC and one EXC row are retained. In source="multi" mode, all positive deltaPSI rows are joined with all negative deltaPSI rows (cartesian join) within each event.

Value

A data.table (or updated ‘SpliceImpactResult‘ when ‘return_class‘ resolves to S4) where each row represents an inclusion-exclusion pair of the same event.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annots <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annots$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annots$sequences)
pairs <- get_pairs(x_seq, source="multi")
print(pairs)
```

---

get_ppi_gene_enrichment *Extract Protein-Interaction-Affected Genes for Enrichment*

Description

Return genes whose splicing affects known protein-protein interactions.

Usage

```
get_ppi_gene_enrichment(hits)
```

Arguments

hits Data frame with PPI annotation columns.

Value

Character vector of gene IDs.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)
ppi <- get_ppi_interactions()
hits_final <- get_ppi_switches(hits_domain, ppi, protein_feature_total)
bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)
enrichment <- get_enrichment(get_ppi_gene_enrichment(hits_final), bg$gene_id, species = 'human', 'ensembl', 'MSig
print(enrichment)
```

---

get_ppi_interactions *Pull PPI from SpliceImpactR's data*

Description

Generation details in inst/scripts

Usage

```
get_ppi_interactions()
```

Value

A ‘data.table‘ of interaction edges used by PPI switching utilities.

Examples

```
ppi_int <- get_ppi_interactions()
print(ppi_int)
```

`get_ppi_switches` *Annotate hits_domain with PPI changes for inclusion vs exclusion forms*

Description

Adds list-cols case_ppi/control_ppi (partner genes) plus counts. Also returns (optionally useful) per-event token sets in PFAM + ELM forms.

Usage

```
get_ppi_switches(
  hits_domain,
  ppi,
  protein_feature_total,
  return_class = c("auto", "data.table", "S4")
)
```

Arguments

`hits_domain`	data.table with gene_id and list-cols case_only_domains_list / control_only_domains_list
`ppi`	wide interaction table from saved data (get_ppi)
`protein_feature_total`	table with database/clean_name/feature_id for interpro mapping
`return_class`	Character. Output mode: ‘"data.table"‘, ‘"S4"‘, or ‘"auto"‘ (default). In ‘auto‘, S4 input returns updated S4 output.

Value

A ‘data.table‘ identical to ‘hits_domain‘ with added columns (or updated ‘SpliceImpactResult‘ when ‘return_class‘ resolves to S4):

‘case_ppi‘, ‘control_ppi‘ Lists of partner transcripts unique to inclusion or exclusion isoforms.

‘n_control_ppi‘, ‘n_control_ppi‘ Counts of gained/lost interactions.

‘n_ppi‘ Total PPI changes (sum of both directions).

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
```

```
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)

bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)
ppi <- get_ppi_interactions()
hits_ppi <- get_ppi_switches(hits_domain, ppi, protein_feature_total)
print(hits_ppi)
hits_ppi[n_ppi > 0, .(event_id, gene_id, n_case_ppi, n_control_ppi, n_ppi, case_ppi, control_ppi)]
```

---

get_protein_features *External function to fetch protein features from biomaRt*

Description

Here we also remove any duplicate and overlapping domains We also add the genomic location to the name of the protein feature for downstream safeguarding and precision. This is to prevent different occurences of the same domain being called as the same in domain identification and enrichment.

Usage

```
get_protein_features(
  biomaRt_databases = c("interpro", "mobidblite", "seg", "ncoils", "tmhmm", "signalp",
    "elm", "gene3d", "pfam"),
  gtf_df,
  sequences = NULL,
  load_path = NULL,
  save_path = NULL,
  base_dir = NULL,
  use_cache = TRUE,
  force_refresh = FALSE,
  timeout = 600,
  ensembl_mirror = NULL,
  species = c("human", "mouse"),
  release = 109,
  test = FALSE,
  combine_overlaps = FALSE
)
```

Arguments

biomaRt_databases
: choose what biomaRt attribute to access, defaulting to interpro, mobidblite, seg, ncoils, tmhmm, signalp

gtf_df
: annotations from get_annotation()

sequences
: only necessary if loading SLiMs from elm get_annotation() (default "sequences") output

load_path
: path to load prior protein features from

save_path
: path to save prior protein features from

base_dir
: Optional cache root. If ‘NULL‘ (default), uses package cache under ‘tools::R_user_dir("SpliceImpactR", "cache")‘.

use_cache
: Logical; if ‘TRUE‘ (default), cache and reuse final ‘get_protein_features()‘ outputs through BiocFileCache.

force_refresh
: Logical; if ‘TRUE‘, recompute and overwrite any existing BiocFileCache entry for this parameter/input signature.

timeout
: ability to extend timeout if biomaRt is not cooperating

ensembl_mirror
: Optional Ensembl mirror to try first for BioMart connections; one of ‘"useast"‘, ‘"www"‘, or ‘"asia"‘. If ‘NULL‘, mirrors are tried in fallback order when ‘release = NULL‘. If a specific ‘release‘ is provided, biomaRt ignores mirror selection.

species
: Character string giving the Ensembl BioMart dataset (default "human"). For mouse, use "mouse".

release
: Release version from Ensembl associated with the GENCODE version used in [get_annotation()]. See the GENCODE human/mouse release listings to map GENCODE and Ensembl versions.

test
: Logical; bool for whether to load from reduced test set.

combine_overlaps
: simplifies protein feature output and combines protein features with the same ID and overlapping coords. Sometimes not desireable

Value

A ‘data.table‘ with one row per protein feature and transcript coupling

Examples

```
annotation_df <- load_example_data("annotation_df")$annotation_df
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, annotation_df$sequences, tim
print(interpro_features)
```

get_proximal_shift_from_hits   *Classify splicing events as proximal or distal*

Description

Determines whether inclusion/exclusion events correspond to proximal or distal terminal exon usage for **AFE** (Alternative First Exon) and **ALE** (Alternative Last Exon) events, based on genomic coordinates and strand orientation.

Usage

```
get_proximal_shift_from_hits(hits)
```

Arguments

hits   ‘data.frame‘ or ‘data.table‘ containing at least:

- ‘event_id‘
- ‘event_type‘
- ‘strand‘
- ‘inc_case‘, ‘inc_control‘
- ‘delta_psi_case‘, ‘delta_psi_control‘

Details

The function compares the genomic coordinates of the inclusion (‘inc_case‘) and exclusion (‘inc_control‘) segments per event:

- For **AFE** events, proximal = exon with smaller start coordinate on the ‘+‘ strand (or larger end on ‘-‘ strand).
- For **ALE** events, proximal = exon with smaller start coordinate on the ‘+‘ strand (or larger end on ‘-‘ strand).

Events outside these types are labeled ‘"nonTerminal"‘.

If `plot = TRUE`, a summary donut chart is printed showing the proportion of proximal vs distal usage per event type.

Value

A ‘data.table‘ identical to ‘hits‘ with an additional column (named ‘V1‘) specifying ‘"proximal"‘, ‘"distal"‘, ‘"overlap"‘, or ‘"nonTerminal"‘.

See Also

[plot_prox_dist()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
proximal_output <- get_proximal_shift_from_hits(pairs)
print(proximal_output)
```

`get_rmats` *Expand rMATS event tables into scalar exon inclusion/exclusion coordinates.*

Description

Converts rMATS "event" tables (SE, MXE, A3SS, A5SS, RI) into standardized scalar representations with explicit inclusion/exclusion segments for downstream genomic mapping.

Usage

```
get_rmats(DT)
```

Arguments

`DT`	A 'data.table' or 'data.frame' of rMATS output (merged or per-sample).

Details

Handles all five canonical rMATS event types (SE, MXE, A3SS, A5SS, RI), applying strand-aware logic for MXE and coordinate adjustments for A3/A5. Non-standard columns (e.g. IJC_SAMPLE_1) are checked for presence.

Value

A standardized 'data.table' containing:

- event_id unique event identifier.
- event_type rMATS event type (SE, MXE, etc.).
- form inclusion/exclusion form.
- gene_id, chr, strand.
- inc, exc scalar genomic segments (string: e.g. '"100-200;300-400"').
- inclusion_reads, exclusion_reads, psi - numeric metrics.
- condition, sample, source_file - carried forward if present.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
rmats <- get_rmats(load_rmats(sample_frame, use = "JCEC", event_types = c("MXE", "SE", "A3SS", "A5SS", "RI")))
print(rmats)
```

---

get_rmats_hit *Wrapper function to get both rmats and hit index cleanly*

Description

Wrapper function to get both rmats and hit index cleanly

Usage

```
get_rmats_hit(
  sample_frame,
  event_types = c("ALE", "AFE", "MXE", "SE", "A3SS", "A5SS", "RI"),
  use = "JCEC",
  keep_annotated_first_last = TRUE
)
```

Arguments

`sample_frame`	Data.frame with columns: `path`, `condition`, and `sample_name`.
`event_types`	event types to load from rMATS
`use`	Character scalar, one of `"JC"` or `"JCEC"`.
`keep_annotated_first_last`	Logical; if TRUE, retain only annotated first/last exons and normalize PSI.

Value

a ‘data.table‘ for all the event types desired from the paths supplied contains: event_id (unique id for event), event_type (AS event type), form (INC/EXC), gene_id (ensembl id), strand, inc, exc (inclusion and exclusion coords) inclusion reads, exclusion reads, psi, sample, condition, source file

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
data <- get_rmats_hit(sample_frame, event_types = c("ALE", "AFE", "MXE", "SE", "A3SS", "A5SS", "RI"))
print(data)
```

get_rmats_post_di *Import post-differential-inclusion rMATS results*

Description

This function reads post-DI rMATS results and converts them into the standardized SpliceImpactR long format with one row per event x (INC/EXC) form.

Input can be: * a data.frame with columns ‘path‘, ‘grp1‘, ‘grp2‘, ‘event_type‘, in which case each file is read and processed; or * a single rMATS results data.frame, in which case ‘event_type‘ must be supplied.

For each event, the function constructs paired INC and EXC entries: * ‘inc‘ contains genomic segments included in the form * ‘exc‘ contains the excluded segment(s) * ‘delta_psi‘, ‘p.value‘, and ‘padj‘ are assigned using the rMATS-reported values

Event IDs are automatically generated (event_type:N) if not supplied

Usage

```
get_rmats_post_di(input, event_type = NULL)
```

Arguments

`input`	Either: * a data.frame with columns ‘path‘, ‘grp1‘, ‘grp2‘, ‘event_type‘, or * a data.frame of rMATS post-DI results.
`event_type`	Optional event type when ‘input‘ contains a single rMATS data.frame. Ignored when file metadata table is supplied.

Value

A ‘data.table‘ with columns:

event_id unique event identifier

event_type splicing event type

form `"INC"` or `"EXC"`

gene_id gene ID

chr chromosome

strand strand

inc genomic coordinates of included segment(s)

exc genomic coordinates of excluded segment(s)

p.value rMATS p-value

padj FDR

delta_psi signed PSI change (+INC, -EXC)

Examples

```
# # Multiple files
# input <- data.frame(
#   path = c('/path/A3SS.MATS.JC.txt', '/path2/A5SS.MATS.JC.txt'),
#   grp1 = c("WT","WT"),
#   grp2 = c("KO","KO"),
#   event_type = c("A3SS", "A5SS")
# )
# res <- get_rmats_post_di(meta)

# Single rMATS table already loaded as df
df <- data.frame(
  ID = 1L,
  GeneID = "ENSG00000182871",
  geneSymbol = "COL18A1",
  chr = "chr21",
  strand = "+",
  longExonStart_0base = 45505834L,
  longExonEnd = 45505966L,
  shortES = 45505837L,
  shortEE = 45505966L,
  flankingES = 45505357L,
  flankingEE = 45505431L,
  ID.2 = 2L,
  IJC_SAMPLE_1 = "4,1,0",
  SJC_SAMPLE_1 = "9,12,3",
  IJC_SAMPLE_2 = "0,4,5",
  SJC_SAMPLE_2 = "11,15,15",
  IncFormLen = 52L,
  SkipFormLen = 49L,
  PValue = 0.6967562,
  FDR = 1,
  IncLevel1 = "0.295,0.073,0.0",
  IncLevel2 = "0.0,0.201,0.239",
  IncLevelDifference = -0.024,
  stringsAsFactors = FALSE
)
res2 <- get_rmats_post_di(df, event_type = "A3SS")
print(res2)
```

`get_sequences` *Retrieve transcript and protein sequences (internal)*

Description

Internal helper that calls [load_seq_map()] to obtain transcript and protein sequences for a given GTF annotation and corresponding FASTA files. Used within higher-level SpliceImpactR workflows.

Usage

```
get_sequences(gtf_df, transcript_path, translation_path)
```

Arguments

`gtf_df` A `data.frame` or `data.table` containing GTF annotation data, typically from [load_gtf_long()].

`transcript_path` Path to the transcript FASTA file (e.g. `gencode.v45.pc_transcripts.fa.gz`).

`translation_path` Path to the protein translation FASTA file (e.g. `gencode.v45.pc_translations.fa.gz`).

Value

A `data.table` with gene, transcript, and protein IDs and their corresponding nucleotide and amino acid sequences.

---

get_splicing_impact *End-to-end SpliceImpactR wrapper with selectable output class*

Description

Runs the core SpliceImpactR pipeline from raw event table (or sample paths) through paired domain/PPI calls, then returns either a compact ‘data.table‘ bundle (‘data‘, ‘res‘, ‘hits_final‘) or an S4 [SpliceImpactResult].

Usage

```
get_splicing_impact(
  sample_frame = NULL,
  data = NULL,
  res = NULL,
  annotation_df = NULL,
  protein_feature_total = NULL,
  exon_features = NULL,
  ppi = NULL,
  source_data = c("rmats_hit", "hitindex", "rmats", "both"),
  event_types = c("ALE", "AFE", "MXE", "SE", "A3SS", "A5SS", "RI", "HFE", "HLE"),
  use = "JCEC",
  keep_annotated_first_last = FALSE,
  min_total_reads = 10L,
  minimum_proportion_containing_event = 0.5,
  terminal_fill = "event_max",
  cooks_cutoff = "Inf",
  adjust_method = "fdr",
  fdr_threshold = 0.05,
```

```
  delta_psi_threshold = 0.1,
  parallel_glm = TRUE,
  chunk_size_glm = 1000L,
  BPPARAM = BiocParallel::SerialParam(),
  chunk_size_match = 2000L,
  source_pairs = c("multi", "paired"),
  show_protein_domains = FALSE,
  return_class = c("data.table", "S4"),
  debug_steps = FALSE,
  metadata = list(),
  verbose = TRUE
)
```

Arguments

`sample_frame` Optional sample manifest for [get_hitindex()] / [get_rmats_hit()]. Must include ‘path‘, ‘condition‘, and optional ‘sample_name‘.

`data` Optional precomputed raw event-level table.

`res` Optional precomputed differential inclusion table.

`annotation_df` Optional annotation list from [get_annotation()] with ‘annotations‘ and ‘sequences‘.

`protein_feature_total` Optional protein feature table from [get_comprehensive_annotations()]. Required if ‘exon_features‘ is not supplied and domain/PPI steps are run.

`exon_features` Optional precomputed exon-feature overlap table from [get_exon_features()].

`ppi` Optional preloaded PPI table. If ‘NULL‘, [get_ppi_interactions()] is used when needed.

`source_data` Which ingestion route to use when ‘data‘ is ‘NULL‘. One of ‘"hitindex"‘, ‘"rmats"‘, ‘"both"‘, or legacy alias ‘"rmats_hit"‘.

`event_types` Event types for [get_rmats_hit()] / [load_rmats()]. Use both terminal and non-terminal types for ‘source_data = "both"‘.

`use` Junction count mode for rMATS ingestion (‘"JC"‘ or ‘"JCEC"‘).

`keep_annotated_first_last` Passed to [get_hitindex()] for terminal events.

`min_total_reads` Passed to [get_differential_inclusion()].

`minimum_proportion_containing_event` Passed to [get_differential_inclusion()].

`terminal_fill` Passed to [get_differential_inclusion()].

`cooks_cutoff` Passed to [get_differential_inclusion()].

`adjust_method` Passed to [get_differential_inclusion()].

`fdr_threshold` Passed to [keep_sig_pairs()] as the adjusted p-value cutoff.

`delta_psi_threshold` Passed to [keep_sig_pairs()] as the absolute delta-psi cutoff.

`parallel_glm` Passed to [get_differential_inclusion()].

`chunk_size_glm` Passed to [get_differential_inclusion()].

`BPPARAM` Passed to [get_differential_inclusion()]. Use a [BiocParallel::BiocParallelParam-class] object (for example [BiocParallel::SerialParam()], [BiocParallel::SnowParam()], or [BiocParallel::MulticoreParam()]).

`chunk_size_match` Chunk size for [get_matched_events_chunked()].

`source_pairs` Pairing mode for [get_pairs()] (‘"multi"‘ or ‘"paired"‘).

`show_protein_domains` Passed to [get_domains()].

`return_class` One of ‘"data.table"‘ or ‘"S4"‘.

`debug_steps` Logical; if ‘TRUE‘, includes intermediates (‘matched‘, ‘hits_sequences‘, ‘pairs‘, ‘seq_compare‘, ‘hits_domain‘) in data.table mode.

`metadata` Optional list attached to ‘SpliceImpactResult@metadata‘.

`verbose` Logical; emit progress messages.

Value

If ‘return_class = "data.table"‘, returns a named list with ‘data‘, ‘res‘, and ‘hits_final‘.

If ‘return_class = "S4"‘, returns a [SpliceImpactResult] containing ‘raw_events‘, ‘di_events‘, and ‘paired_hits‘ slots.

Examples

```
ex <- load_example_data(
  c("sample_frame", "annotation_df", "protein_feature_total", "ppi")
)
out <- get_splicing_impact(
  sample_frame = ex$sample_frame,
  annotation_df = ex$annotation_df,
  protein_feature_total = ex$protein_feature_total,
  ppi = ex$ppi,
  source_data = "rmats",
  event_types = c("SE"),
  use = "JCEC",
  parallel_glm = FALSE,
  BPPARAM = BiocParallel::SerialParam(),
  verbose = FALSE
)
print(names(out))
```

`get_user_data` *Get User-Supplied Splicing Event Data*

Description

SpliceImpactR accepts user-supplied splicing data in the same structure produced by `get_rmats_hit()`. Each event must be represented at the event-form and sample level.

Event representation - Each splicing event must be split into two forms: - `INC`: the inclusion isoform - `EXC`: the exclusion isoform - Alternative first/last exon events (AFE/ALE) or more abstract events may instead provide a single `SITE` form.

Coordinates - `inc` column: genomic coordinates included in the given form - `exc` column: genomic coordinates excluded in the given form - Coordinates may be one or multiple ranges (e.g., "100-200" or "100-150;300-350") - User must supply at least an inc and if supplying an exc, accompany with an inc coord

Counts and PSI - `inclusion_reads` and `exclusion_reads` must be provided per form - `psi` must be provided per sample (range 0-1) If psi isn't given, it will be extracted through `inclusion_reads/exclusion_reads`

Sample structure - Each event must have `INC` and `EXC` rows (or just `SITE`) - Each event must have >1 sample per condition (e.g., case vs control) - Required sample annotations: `sample`, `condition`

Required columns `event_id`, `event_type`, `form`, `gene_id`, `chr`, `strand`, `inc`, `exc`, `inclusion_reads`, `exclusion_reads`, `psi`, `sample`, `condition`

Defaults - If `event_type` not supplied: filled as `"unknown"` - If `source_file` not supplied: filled with empty string

This format enables downstream functionality including PSI modeling, annotation integration, and protein consequence prediction.

Usage

```
get_user_data(df)
```

Arguments

`df`	Data frame with splicing events. Detailed in description

Value

data.table with cols, detailed above: "event_id","event_type","form", "gene_id","chr", "strand", "inc","exc","inclusion_reads","exclusion_reads", "psi", "sample", "condition","source_file" – designed to match get_rmats_hit output

Examples

```
example_df <- data.frame(
  event_id = rep("A3SS:1", 8),
  event_type = "A3SS",
```

```
  form = rep(c("INC","EXC"), each = 4),
  gene_id = "ENSG00000158286",
  chr = "chrX",
  strand = "-",
  inc = c(rep("149608626-149608834",4), rep("149608626-149608829",4)),
  exc = c(rep("",4), rep("149608830-149608834",4)),
  inclusion_reads = c(30,32,29,31, 2,3,4,3),
  exclusion_reads = c(1,1,2,1, 28,27,26,30),
  sample = c("S1","S2","S3","S4","S1","S2","S3","S4"),
  condition = rep(c("case","case","control","control"), 2),
  stringsAsFactors = FALSE
)
example_df$psi < example_df$inclusion_reads / example_df$exclusion_reads
user_data <- get_user_data(example_df)
print(user_data)
```

`get_user_data_post_di` *Format user-supplied post-DI (post-differential-inclusion) splicing results*

Description

This function converts user-supplied event results into the internal SpliceImpactR DI format. It accepts per-event statistics and ensures each splicing event contains valid inclusion/exclusion structure.

Requirements **Event representation** - Each splicing event must be split into two forms: - `INC`: the inclusion isoform - `EXC`: the exclusion isoform - Alternative first/last exon events (AFE/ALE) or more abstract events may instead provide a single `SITE` form.

Coordinates - `inc` column: genomic coordinates included in the given form - `exc` column: genomic coordinates excluded in the given form - Coordinates may be one or multiple ranges (e.g., "100-200" or "100-150;300-350")

- User **must supply ‘event_id‘** (unique ID per splicing event, event_id = event_type:x for form != SITE. event_id = gene:event_type for form = SITE. Look at example output from get_differential_inclusion using test data for more examples) - Each event must be either: - **INC + EXC** forms (paired isoforms), or - **SITE** (single isoform) - Required columns: ‘gene_id, chr, strand, inc, exc, form, event_id‘

Behavior - Does **not** generate event IDs: user must provide them - Constructs ‘site_id = event_type|gene_id|chr|inc|exc|form‘ - ‘delta_psi‘: - If missing: INC = +1, EXC = -1, SITE expands to +1 and -1 each to get all relevant comparisons - ‘p.value‘, ‘padj‘: - If missing: set to 0 - All diagnostic fields (‘cooks_max, n, n_used, n_samples, n_case, mean_psi_ctrl, mean_psi_case, n_control‘) set to -1 if missing

Validation - Throws error if: - Any event lacks **INC+EXC** or **SITE** - An event mixes SITE with INC/EXC

Output Returns a ‘data.table‘ formatted like SpliceImpactR DI output. Ready for annotation, pairing, enrichment, and PPI analysis.

Usage

```
get_user_data_post_di(df)
```

Arguments

df	Data frame of post-DI results, detailed in description

Value

A data.table formatted like SpliceImpactR DI output (get_differential_inclusion)

Examples

```
example_user_data <- data.frame(
  event_id = rep("A3SS:1", 8),
  event_type = "A3SS",
  gene_id = "ENSG00000158286",
  chr = "chrX",
  strand = "-",
  form = rep(c("INC","EXC"), each = 4),
  inc = c(
    rep("149608626-149608834", 4),
    rep("149608626-149608829", 4)
  ),
  exc = c(
    rep("", 4),
    rep("149608830-149608834", 4)
  ),
  inclusion_reads = c(30, 28, 25, 32,  2, 3, 4, 3),
  exclusion_reads = c(1, 2, 1, 1, 28, 27, 26, 30),
  sample = c("S1","S2","S3","S4","S1","S2","S3","S4"),
  condition = rep(c("case","case","control","control"), 2),
  stringsAsFactors = FALSE
)

# compute psi if missing, just for demo

post_di_user_data <- get_user_data_post_di(example_user_data)
print(post_di_user_data)
```

---

identify_hybrid_exons_split
Identify potential hybrid exons (internal)

Description

Internal helper to find exons that overlap between internal and terminal (first/last) exons of different transcripts within the same gene. Used to detect possible hybrid exon configurations.

Usage

```
identify_hybrid_exons_split(gtf_df)
```

Arguments

`gtf_df`	A `data.frame` or `data.table` containing GTF annotations with `gene_id`, `transcript_id`, `exon_id`, `chr`, `start`, `end`, and `absolute_exon_class`.

Details

Uses **data.table::foverlaps()** to identify exons that share genomic coordinates but belong to different transcripts within the same gene.

Value

A list of two `data.tables`:

- `first_hybrids` overlaps between first and internal exons
- `last_hybrids` overlaps between last and internal exons

Each includes transcript IDs, exon IDs, and mapped transcript `row_uids`.

---

import_di_table *Standardize a differential inclusion (DI) result table*

Description

Converts an arbitrary differential inclusion result table into the standardized column format expected by SpliceImpactR functions.

Usage

```
import_di_table(
  df,
  colmap = list(gene_id = "gene_id", chr = "chr", strand = "strand", inc = "inc", exc =
    "exc", delta_psi = "delta_psi", pvalue = "p.value", event_type = NULL),
  default_event_type = "SITE",
  adjust_method = "fdr",
  add_chr_prefix = FALSE
)
```

Arguments

df	A ‘data.frame‘ or ‘data.table‘ containing differential inclusion results.
colmap	A named list mapping required fields in ‘df‘ to standard names (‘gene_id‘, ‘chr‘, ‘strand‘, ‘inc‘, ‘exc‘, ‘delta_psi‘, ‘pvalue‘, and optionally ‘event_type‘).
default_event_type	Character. Default ‘event_type‘ to assign if none provided (default ‘"SITE"‘).
adjust_method	Character. Multiple-testing correction method passed to [stats::p.adjust()] (default ‘"fdr"‘).
add_chr_prefix	Logical. Add ‘"chr"‘ prefix if absent (default ‘FALSE‘).

Details

This function provides a uniform interface for importing external DI results (e.g. from rMATS, MAJIQ, or SUPPA2) so they can be compared or plotted alongside SpliceImpactR outputs.

Value

A standardized ‘data.table‘ with columns: ‘site_id‘, ‘event_type‘, ‘gene_id‘, ‘chr‘, ‘strand‘, ‘inc‘, ‘exc‘, ‘delta_psi‘, ‘p.value‘, ‘padj‘, and ‘form‘.

Examples

```
df <- data.frame(
  gene_id = "ENSG00000280071",
  chr = "7",
  strand = "+",
  inc = "1940088-1940549",
  exc = "",
  delta_psi = 0.25,
  p.value = 0.01
)
di_std <- import_di_table(df)
head(di_std)
```

---

integrated_event_summary

Integrated summary of event classification, alignment, and domain changes

---

Description

Provides a comprehensive visualization and summary of event classification outcomes (frame shifts, rescues, matches, etc.), alignment quality, and domain change prevalence across alternative splicing event types. Integrates results from [‘compare_sequence_frame()‘] with pre-filter event tables to display pre- vs post-filter usage, event coordination, and gene/domain overlaps.

Usage

```
integrated_event_summary(hits, pre_filter_hits)
```

Arguments

`hits`	‘data.frame‘, ‘data.table‘, or ‘SpliceImpactResult‘ output from [‘compare_sequence_frame()‘], containing per-event alignment and domain information (e.g. ‘summary_classification‘, ‘prot_score‘, ‘event_type‘, ‘case_only_n‘, ‘control_only_n‘, etc.).
`pre_filter_hits`	‘data.frame‘, ‘data.table‘, or ‘SpliceImpactResult‘ representing the unfiltered input events (e.g. raw differential inclusion table prior to sequence comparison).

Details

The function integrates multiple layers of event-level characterization:

- Event-type composition and class proportions
- Protein alignment quality distribution
- Domain-change prevalence (case/control/both)
- Event-type coordination heatmap (Jaccard similarity across genes)
- Relative event retention pre- vs post-filtering

Value

A named list with:

‘summaries‘ List containing per-type tables: `by_type`, `class_counts`, `score_summary`, `domain_prevalence`, and `relative_use`.

‘plot‘ A multi-panel [‘patchwork‘] composite summarizing classification, alignment, domain changes, and coordination.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)
```

```
ppi <- get_ppi_interactions()
hits_final <- get_ppi_switches(hits_domain, ppi, protein_feature_total)
int_summary <- integrated_event_summary(hits_final, res)
print(int_summary)
```

`ipr_to_pfam` *Convert InterPro IDs to PFAM IDs*

Description

Convert InterPro IDs to PFAM IDs

Usage

```
ipr_to_pfam(ipr_ids)
```

Arguments

`ipr_ids`	Character vector of InterPro IDs (for example, ‘"IPR000719"‘).

Value

Character vector of PFAM IDs mapped from ‘ipr_ids‘.

`keep_sig_pairs` *Filter event pairs by significance and deltaPSI thresholds*

Description

Keeps all rows belonging to events where at least one isoform or site passes adjusted p-value and deltaPSI significance criteria.

Usage

```
keep_sig_pairs(
  DT,
  padj_thr = 0.05,
  dpsi_thr = 0.1,
  return_class = c("auto", "data.table", "S4")
)
```

Arguments

DT	A ‘data.frame‘ or ‘data.table‘ containing at least ‘event_id‘, ‘padj‘, and ‘delta_psi‘ columns.
padj_thr	Numeric. Adjusted p-value threshold (default ‘0.05‘).
dpsi_thr	Numeric. Absolute deltaPSI threshold (default ‘0.1‘).
return_class	Character. Output mode: ‘"data.table"‘, ‘"S4"‘, or ‘"auto"‘ (default). In ‘auto‘, S4 input returns updated S4 output.

Value

A ‘data.table‘ (or updated ‘SpliceImpactResult‘ when ‘return_class‘ resolves to S4) containing all rows from event pairs in which at least one row meets the significance criteria.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
sig_di <- keep_sig_pairs(res)
print(sig_di)
```

---

load_example_data   *Load bundled example inputs for documentation*

Description

Returns commonly used example objects (sample manifest, test annotations, optional feature mappings, optional PPI table) so man-page examples can stay focused on the documented function rather than setup boilerplate.

Usage

```
load_example_data(
  include = c("sample_frame", "annotation_df"),
  biomaRt_databases = c("interpro"),
  test = TRUE
)
```

Arguments

include	Character vector selecting which objects to return. Supported values are ‘"sample_frame"‘, ‘"annotation_df"‘, ‘"protein_feature_total"‘, ‘"exon_features"‘, ‘"ppi"‘, and ‘"all"‘. If ‘"all"‘ is present, it expands to ‘c("sample_frame", "annotation_df", "protein_feature_total", "exon_features")‘.

biomaRt_databases
: Character vector passed to [get_protein_features()] when protein features are requested. Default is ‘"interpro"‘.

test
: Logical passed to [get_protein_features()] (default ‘TRUE‘).

Value

Named list containing the requested objects.

Examples

```
ex <- load_example_data(c("sample_frame", "annotation_df"))
sample_frame <- ex$sample_frame
annotation_df <- ex$annotation_df

ex2 <- load_example_data(c("annotation_df", "exon_features"))
exon_features <- ex2$exon_features
print(exon_features)
```

---

load_gtf_long *Load a GTF file into a long-form data.table (internal)*

Description

Internal helper to read a GTF or GFF file (optionally gzipped) and return it as a tidy **data.table**. Ensures consistent column naming, fills in missing identifiers from the ‘attributes‘ column, and optionally adds a unique row identifier.

Usage

```
load_gtf_long(gtf_path_or_df, add_row_uid = TRUE)
```

Arguments

gtf_path_or_df
: Character string giving the path or URL to a GTF/GFF file (optionally prefixed with ‘file://‘), or an existing `data.frame`/`data.table` containing GTF-like data.

add_row_uid
: Logical; if ‘TRUE‘, adds a unique ‘row_uid‘ column for reference.

Details

The function uses **rtracklayer** to import GTF/GFF files, which returns an S4 `DataFrame`. It is then coerced to a standard `data.table`. When certain ID columns are missing, they are extracted from the ‘attributes‘ column using [attr_get()].

Value

A `data.table` with standardized GTF fields and a consistent set of identifier columns.

Examples

```
## Not run:
gtf_dt <- load_gtf_long("gencode.v45.annotation.gtf.gz")
data.table::head(gtf_dt)

## End(Not run)
```

`load_rmats` *Load rMATS event files into standardized data.tables*

Description

Parses rMATS output (.MATS.JC.txt or .MATS.JCEC.txt) for multiple event types and returns unified event tables ready for downstream inclusion/exclusion processing.

Usage

```
load_rmats(
  paths,
  use = c("JC", "JCEC"),
  event_types = c("SE", "RI", "A5SS", "A3SS", "MXE")
)
```

Arguments

`paths`	A data.frame with columns `path`, `sample_name`, and `condition`.
`use`	Character scalar, one of `"JC"` or `"JCEC"`.
`event_types`	Event types to include: one or more of `c("SE", "RI", "A5SS", "A3SS", "MXE")`.

Value

A ‘data.table‘ with unified rMATS event annotations, including columns:

- event_type, event_id, gene_id, chr, strand
- sample, condition (if applicable)
- delta_psi, pvalue, fdr (if present)
- inclusion/exclusion read counts

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
rmats <- load_rmats(sample_frame, use = "JCEC", event_types = c("MXE", "SE", "A3SS", "A5SS", "RI"))
print(rmats)
```

`load_seq_map` *Build a compact transcript protein sequence map (internal)*

Description

Internal helper that integrates information from a GTF, transcript FASTA, and protein FASTA to produce a compact mapping of genes, transcripts, and proteins, optionally including nucleotide and amino-acid sequences.

Usage

```
load_seq_map(
  gtf_df,
  txfa_path,
  aafa_path,
  take_tx_cds_slice = TRUE,
  keep_sequences = TRUE,
  add_row_uids = TRUE
)
```

Arguments

`gtf_df`	A `data.frame` or `data.table` produced by [load_gtf_long()], containing at least `gene_id`, `transcript_id`, `protein_id`, and optionally `row_uid`.
`txfa_path`	Character string giving the path to the GENCODE transcript FASTA file (e.g. `gencode.v45.pc_transcripts.fa.gz`).
`aafa_path`	Character string giving the path to the GENCODE protein FASTA file (e.g. `gencode.v45.pc_translations.fa.gz`).
`take_tx_cds_slice`	Logical; if `TRUE`, restricts transcript sequences to their coding region based on the `CDS:start-end` annotation in the FASTA header.
`keep_sequences`	Logical; if `TRUE`, include sequence strings in the output table, otherwise store `NA_character_`.
`add_row_uids`	Logical; if `TRUE`, attaches corresponding `row_uids` for genes and transcripts from `gtf_df`.

Details

The function combines identifiers from GTF features, transcript FASTA headers, and protein FASTA headers to construct a unified mapping. It uses **Biostrings** to load FASTA data and **data.table** for efficient joins.

Value

A `data.table` containing, for each transcript:

row_uid Row index within the output mapping.

gene_id, transcript_id, protein_id Identifiers from GENCODE.

transcript_seq, protein_seq Optional sequence strings.

gene_row_uid, transcript_row_uid Original UID references (if added).

---

mark_changing_partners_split

Helper to annotate PPI changes from DDI and DMI

Description

Helper to annotate PPI changes from DDI and DMI

Usage

```
mark_changing_partners_split(
  ppi,
  gene_id,
  changed_pfam_case,
  changed_pfam_control,
  changed_motif_case = character(),
  changed_motif_control = character()
)
```

---

match_events_to_annotations_vec

Match alternative splicing events to annotated exons and transcripts

---

Description

Performs vectorized overlap mapping between event coordinates (e.g. inclusion or exclusion intervals) and exons from an annotation resource. Returns the best-matching transcript and exon set per event based on coverage, exon classification, and protein-coding preference.

Usage

```
match_events_to_annotations_vec(events, annotations, minOverlap = 0.05)
```

Arguments

`events` A ‘data.frame‘ or ‘data.table‘ containing splicing events with columns ‘chr‘, ‘strand‘, ‘gene_id‘, and coordinate fields ‘inc‘ and ‘exc‘ (semicolon-delimited ‘"start-end"‘ strings).

`annotations` A gene annotation table (e.g. from [rtracklayer::import()] on a GTF file) with exon and transcript rows, passed to [build_from_annotations()].

`minOverlap` Minimum fractional overlap (0-1) required between an inclusion segment and an annotated exon to count as a hit. Default ‘0.05‘.

Details

The function uses [GenomicRanges::findOverlaps()] to match event inclusion intervals to exons. Candidate transcripts are filtered to ensure sufficient coverage and absence of overlaps with exclusion coordinates.

The algorithm prioritizes exon classification (‘first‘, ‘internal‘, ‘last‘) consistent with the event type (AFE, ALE, SE, etc.), followed by reciprocal overlap fractions, intersection width, and protein-coding status.

Value

A ‘data.table‘ containing one row per input event with the following appended columns:

‘transcript_id‘ The best matching transcript ID.

‘exons‘ Semicolon delimited list of exon IDs covered by the event.

‘inc_exons_by_idx‘ Semicolon delimited exon IDs per inclusion index (maintaining order).

‘inc_rows_by_idx‘ Semicolon delimited exon row indices matching inclusion order.

`overview_spicing_comparison`

Overview of global splicing event distributions between conditions

---

Description

Generates a multi-panel comparison summarizing global splicing characteristics (event counts, events-per-gene, PSI distributions) between experimental and control conditions, normalized by sequencing depth.

Usage

```
overview_spicing_comparison(
  events,
  sample_df,
  depth_norm = c("exon_files", "user-given"),
  event_type = "AFE",
  conditions = c(control = "control", experimental = "case"),
  minReads = 10,
  output_file = NULL
)
```

Arguments

events	‘data.frame‘ or ‘data.table‘ of splicing events with at least: ‘sample‘, ‘condition‘, ‘gene_id‘, ‘inclusion_reads‘, ‘exclusion_reads‘, ‘psi‘, ‘inc‘, ‘exc‘.
sample_df	Metadata ‘data.frame‘ with sample-level paths and conditions.
depth_norm	Normalization mode: ‘’exon_files’‘ (compute from read files) or ‘’user-given’‘ (use provided size factors).
event_type	Character string specifying the event class (e.g., ‘"AFE"‘, ‘"ALE"‘).
conditions	Named character vector mapping ‘control‘ and ‘experimental‘ condition labels.
minReads	Minimum reads required for inclusion or exclusion (default = 10).
output_file	Optional path to save a combined summary figure.

Details

The output combines: - **Panel A:** Depth-normalized event counts per sample (Wilcoxon test) - **Panel B:** Mean events per gene per sample (Wilcoxon test) - **Panel D:** PSI cumulative distribution comparison (K-S test)

Size factors are computed internally using [.get_size_factors_from_exons()], enabling robust normalization.

Value

Invisibly returns a combined [‘patchwork‘] plot object.

See Also

[.get_size_factors_from_exons()], [getSizeFactors()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
ov <- overview_spicing_comparison(hit_index, sample_frame, 'exon_files')
print(ov)
```

---

plot_alignment_summary

Plot alignment score distribution and coding summary

Description

Visualizes alignment scores (‘prot_pid‘ or ‘dna_pid‘) and coding class composition of hits, showing both the categorical composition and histogram of alignment identity values.

Usage

```
plot_alignment_summary(
  hits,
  mode = c("protein", "transcript"),
  output_file = NULL
)
```

Arguments

hits	‘data.frame‘ or ‘data.table‘ containing ‘prot_pid‘ or ‘dna_pid‘ and ‘summary_classification‘ columns.
mode	Character, either ‘"protein"‘ (uses ‘prot_pid‘) or ‘"transcript"‘ (uses ‘dna_pid‘).
output_file	Optional path to save the combined plot.

Value

A composite ‘ggplot‘ object (from ‘ggpubr::ggarrange‘) showing stacked bar counts by coding class and histogram of alignment identity scores.

See Also

[plot_length_comparison()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
alignment_summary <- plot_alignment_summary(seq_compare)
print(alignment_summary)
```

---

plot_di_volcano_dt *Volcano plot for differential inclusion results*

Description

Generates a volcano plot of deltaPSI vs. -log10(FDR) highlighting significant events.

Usage

```
plot_di_volcano_dt(di, padj_thr = 0.05, dpsi_thr = 0.1)
```

Arguments

`di`	A ‘data.frame‘ or ‘data.table‘ containing at least ‘delta_psi‘ and ‘padj‘ columns (optionally ‘event_type‘).
`padj_thr`	Numeric. Adjusted p-value threshold (default ‘0.05‘).
`dpsi_thr`	Numeric. Absolute deltaPSI threshold (default ‘0.1‘).

Details

Significant sites are colored in ‘deeppink4‘; nonsignificant sites are shown in light grey. Dashed and dotted lines indicate deltaPSI and FDR thresholds.

Value

A ‘ggplot2‘ object showing differential inclusion significance.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
plot_di_volcano_dt(res)
```

---

plot_enriched_domains_counts

Plot enriched domains by associated event count

Description

Visualizes the top enriched protein domains based on the number of events contributing to each domain’s enrichment, optionally coloring by -log10 adjusted p-value.

Usage

```
plot_enriched_domains_counts(enriched_domains, top_n = 25)
```

Arguments

`enriched_domains`	‘data.frame‘ or ‘data.table‘ Output table from [enrich_domains_hypergeo()], including at least columns ‘domain_id‘ and ‘events‘. Optional columns ‘padj‘ and ‘OR‘ are used for coloring and labeling.
`top_n`	Integer (default ‘25‘) Number of top domains to display, ranked by increasing ‘padj‘.

Details

The function expects the output of [enrich_domains_hypergeo()], typically a ‘data.table‘ or ‘data.frame‘ containing ‘domain_id‘, ‘events‘, and optionally ‘padj‘ and ‘OR‘.

Each bar corresponds to one domain, with height proportional to the number of unique ‘event_id‘s contributing to that domain. Bars are ordered by ascending adjusted p-value (‘padj‘), and colored by -log10(padj) if available. When no ‘padj‘ column is present, the bars are shown in a uniform fill color.

Value

A ‘ggplot‘ object showing bars of domain counts colored by enrichment significance.

See Also

[enrich_domains_hypergeo()], [enrich_by_event()], [enrich_by_db()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)
bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)
enriched_domains <- enrich_domains_hypergeo(hits_domain, bg, db_filter = 'interpro')
plot_enriched_domains_counts(enriched_domains, top_n = 20)
```

---

plot_length_comparison

Compare inclusion vs. exclusion isoform lengths

Description

Generates a multi-panel summary comparing isoform lengths between inclusion (INC) and exclusion (EXC) events for either protein or transcript modes.

Usage

```
plot_length_comparison(
  hits,
  phenotypes = c(control = "control", experimental = "case"),
  mode = c("protein", "transcript"),
  output_file = NULL
)
```

Arguments

`hits`	‘data.frame‘ or ‘data.table‘ containing event-level results, including at least ‘prot_len_case‘, ‘prot_len_control‘, and ‘prot_len_diff‘ for ‘mode = "protein"‘, or their transcript analogues ‘tx_len_case‘, ‘tx_len_control‘, and ‘tx_len_diff‘.
`phenotypes`	Named character vector of length 2 giving labels for control and experimental phenotypes. Must have names ‘"control"‘ and ‘"experimental"‘.
`mode`	Character, one of ‘"protein"‘ or ‘"transcript"‘. Determines which length columns to use and whether to derive protein-coding categories.
`output_file`	Optional path for saving the combined plot (e.g., ‘"length_summary.png"‘).

Details

Produces three coordinated panels:

1. Paired boxplot showing INC vs EXC lengths per event with Wilcoxon paired test annotation.
2. Density plot of delta length (INC - EXC).
3. Barplot summarizing protein-coding categories.

Value

A composite ‘ggplot‘ object (assembled with ‘patchwork‘) showing paired boxplots, delta-length density, and protein-coding class distribution.

See Also

[plot_alignment_summary()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
```

```
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)
proximal_output <- plot_length_comparison(seq_compare)
print(proximal_output)
```

---

plot_ppi_summary *Plot summary of altered PPI interactions*

Description

Visualizes the frequency and magnitude of gained/lost PPIs per event, using a dual-panel layout: - left: proportion of events with any PPI change - right: histograms of CASE and CONTROL partner counts (non-zero only)

Usage

```
plot_ppi_summary(
  df,
  bins = 30,
  palette = c(no = "grey80", yes = "deeppink4", CASE = "#2b8cbe", CONTROL = "#e34a33"),
  output_file = NULL,
  width = 9,
  height = 4.8
)
```

Arguments

df	‘data.table‘ or ‘data.frame‘ with PPI counts per event, as returned by [ppi_switches_for_hits()].
bins	Integer; number of histogram bins (default ‘30‘).
palette	Named character vector of fill colors for the plot (default includes ‘"no"‘, ‘"yes"‘, ‘"CASE"‘, ‘"CONTROL"‘).
output_file	Optional path to save the figure (‘.png‘ or ‘.pdf‘).
width, height	Numeric dimensions (in inches) for saved plot.

Value

A ‘ggplot‘ object combining two panels (using ‘patchwork‘).

See Also

[ppi_switches_for_hits()]

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
annotation_df <- load_example_data("annotation_df")$annotation_df
matched <- get_matched_events_chunked(res, annotation_df$annotations, chunk_size = 2000)
x_seq <- attach_sequences(matched, annotation_df$sequences)
pairs <- get_pairs(x_seq, source="multi")
seq_compare <-compare_sequence_frame(pairs, annotation_df$annotations)

annotation_df <- get_annotation(load = 'test')
interpro_features <- get_protein_features(c("interpro"), annotation_df$annotations, timeout = 600, test = TRUE)
protein_feature_total <- get_comprehensive_annotations(list(interpro_features))

exon_features <- get_exon_features(annotation_df$annotations, protein_feature_total)

hits_domain <- get_domains(seq_compare, exon_features)

bg <- get_background(source = "hit_index",
                     input = sample_frame,
                     annotations = annotation_df$annotations,
                     protein_features = protein_feature_total)
ppi <- get_ppi_interactions()
hits_final <- get_ppi_switches(hits_domain, ppi, protein_feature_total)
ppi_plot <- plot_ppi_summary(hits_final)
print(ppi_plot)
```

---

plot_prox_dist *Plot proximal vs distal exon usage*

Description

Creates a donut-style summary plot showing the number of events classified as proximal or distal for each event type (AFE, ALE).

Usage

```
plot_prox_dist(res)
```

Arguments

res	‘data.table‘ output from [get_proximal_shift_from_hits()], containing at least columns ‘event_type‘ and ‘V1‘ (proximal/distal label).

Details

The plot shows each event type as a donut chart:

- Inner label = total number of events.
- Slices = counts of proximal and distal events.

Only event types with at least one valid classification are shown.

Value

A ‘ggplot‘ object (donut-style bar chart).

See Also

[get_proximal_shift_from_hits()]

`plot_two_transcripts_with_domains_unified`

Plot two transcripts with exon structure and protein feature tracks (unified view)

Description

Visualize **two Ensembl transcripts** side-by-side with their exon structures and optional **protein feature/domain tracks** (e.g., InterPro, Pfam, ELM, SEG, SignalP), using a single entrypoint. The plot can be rendered in either:

Usage

```
plot_two_transcripts_with_domains_unified(
  ...,
  view = c("transcript", "protein")
)
```

Arguments

`...` Additional arguments forwarded to the internal workhorse `plot_two_transcripts_with_features()`. Common arguments include:

transcripts Character vector of length 2 of Ensembl transcript IDs.

gtf_df GTF-like exon annotation table containing at least `transcript_id`, `type=="exon"`, `exon_number`, `chr`, `strand`, `start`, `end`.

protein_features Protein feature table with at least `ensembl_transcript_id`, `name`, `feature_id`, `database`.

feature_db Optional character vector of databases to retain (e.g., `c("interpro","pfam","elm","seg",`

wrap_width Integer; width for wrapping long domain labels.

highlight_hits Optional data.frame/data.table of event rows used for highlighting.

highlight_event_id Optional event ID to select from `highlight_hits`.

highlight_alpha Alpha transparency for highlight bands.

highlight_box Logical; draw dashed vertical bounds around highlighted spans.

highlight_box_pad_frac Fraction of total x-range used to pad highlight bounds.

highlight_box_lwd Line width for highlight bounding lines.

combine_domains Logical; combine identical domain labels onto shared tracks.

domain_base_gap Vertical gap between transcript backbone and first domain track.

domain_track_step Vertical spacing between stacked domain tracks.

domain_label_dy Vertical offset used to place domain labels.

`view` Character scalar selecting the visualization coordinate system: `"transcript"` (genomic/intron-aware) or `"protein"` (compact/exonic).

Details

- **Transcript view** (‘view = "transcript"‘): genomic x-axis with introns drawn and, when both transcripts are negative-strand, a strand-aware x-axis reversal so the display reads left-to-right in **5’→3’** direction. - **Protein view** (‘view = "protein"‘): compact, intron-free x-axis where exons are concatenated end-to-end (exonic coordinates), making it easier to compare protein feature locations across isoforms without large genomic intron gaps.

Optionally, event-specific genomic spans (e.g., inclusion/exclusion regions) can be overlaid as translucent highlight bands per transcript.

What gets drawn

- Exons as black rectangles (alternating alpha in protein/compact view).
- Introns as grey connector segments (transcript/genomic view only).
- Protein features as stacked rectangles under each transcript (if present).
- Domain labels anchored to the left edge (or right when the x-axis is reversed).
- Optional highlighted spans with dashed bounding lines.

Protein/domain tracks Protein features are filtered to the two transcripts and optionally filtered by `feature_db`. Features are clipped to exons in transcript/genomic view, and projected into compact/exonic coordinates in protein view.

- If `combine_domains` = `TRUE`, identical domain labels share a common vertical track to reduce redundancy.
- If `combine_domains` = `FALSE`, each feature instance is assigned its own track (potentially more vertical space, but preserves instance-level separation).

Event highlighting If `highlight_hits` and `highlight_event_id` are provided, event spans are parsed from `inc_case`, `exc_case`, `inc_control`, `exc_control` columns. In transcript/genomic view spans are used directly; in protein/compact view spans are projected into compact coordinates per transcript using exon maps.

Value

A `ggplot` object, or `NULL` if no drawable content is available (e.g., when both transcripts have zero features and you have configured internal logic to early-return on missing domains).

Expected input formats

protein_features `name` **column:** The internal parser expects feature genomic coordinates encoded in the `name` field formatted as `"<label>;chr:start-end"` (e.g. `"PF00069;chr7:123-456"`).

highlight_hits span columns: Span columns are expected as strings `"start-end"` using genomic coordinates. Missing spans should be `NA_character_`.

Highlight input (`custom_hits_domain`) example

The `highlight_hits` object is expected to be a table (data.frame/data.table) with at least one row per event. Use `highlight_event_id` to select the row to plot. Required columns are `event_id`, `event_type_control`, `transcript_id_case`, `transcript_id_control`. Span columns may include `inc_case`, `exc_case`, `inc_control`, `exc_control` and should be genomic coordinate strings of the form `"start-end"` (or `NA_character_` when absent).

```
custom_hits_domain <- data.table::data.table(
  event_id = event:n,
  event_type = event,
  transcript_id_case = transcript_id,
  transcript_id_control = transcript_id,
  inc_case = inc_case,
  inc_control = inc_control,
  exc_case = exc_case,
  exc_control = exc_control
)
```

See Also

`ggplot` for rendering and theming.

Examples

```
# Example highlight row (skipped exon / SE), but can usually just use
# hits_domain/hits_final and supply the event_id in highlight_event_id
custom_hits_domain <- data.table::data.table(
  event_id = "AFE:1",
  event_type = "AFE",
  transcript_id_case = "ENST00000337907",
  transcript_id_control = "ENST00000476556",
  inc_case = "8655973-8656441",
  inc_control = "8423561-8423666",
  exc_case = NA,
  exc_control = NA
)
```

```
# Transcript (genomic) view: introns included, strand-aware axis
p_tx <- plot_two_transcripts_with_domains_unified(
  gtf_df = annotation_df$annotations,
  protein_features = protein_feature_total,
  feature_db = c("interpro", "pfam"),
  highlight_hits = custom_hits_domain,
  highlight_event_id = "AFE:1",
  combine_domains = FALSE,
  view = "protein"
)

# Protein (compact) view: introns removed
p_prot <- plot_two_transcripts_with_domains_unified(
  gtf_df = annotation_df$annotations,
  protein_features = protein_feature_total,
  feature_db = c("interpro", "pfam", "elm", "seg"),
  highlight_hits = hits_final,
  highlight_event_id = "ENSG00000142599:AFE",
  combine_domains = TRUE,
  view = "transcript"
)

# We are also able to just probe 2 random transcripts from annotations
p_prot <- plot_two_transcripts_with_domains_unified(
  transcripts = c("ENST00000337907","ENST00000476556"),
  gtf_df = annotation_df$annotations,
  protein_features = protein_feature_total,
  feature_db = c("interpro", "pfam", "elm", "seg"),
  combine_domains = TRUE,
  view = "protein"
)
```

`probe_individual_event` *Visualize PSI values for a single splicing event*

Description

Creates a per-event PSI summary across samples. For **AFE** and **ALE** events, the plot separates PSI by ‘inc‘ entry to distinguish alternative terminal exons; other event types are summarized by ‘event_id‘.

Usage

```
probe_individual_event(data, event, fill_zeros = TRUE)
```

Arguments

data
: ‘data.frame‘ or ‘data.table‘ containing at least the columns ‘event_id‘, ‘event_type‘, ‘psi‘, ‘condition‘, and ‘sample‘. For terminal events, an ‘inc‘ column is also required.

event
: Character scalar specifying the ‘event_id‘ to visualize.

fill_zeros
: Logical indicating whether to fill missing PSI values with zeros for samples that contain any observation of the event (default: ‘TRUE‘).

Value

A list with elements:

- ‘plot‘: ‘ggplot‘ box/point plot of PSI per sample group.
- ‘data‘: ‘data.table‘ used to build the plot.

Examples

```
ex <- load_example_data("sample_frame")
sample_frame <- ex$sample_frame
hit_index <- get_hitindex(sample_frame)
res <- get_differential_inclusion(hit_index)
event_probe <- "ENSG00000117632:AFE"
probe_individual_event(hit_index, event = event_probe)
```

---

prot_hdr_to_enst *Extract transcript identifier from protein FASTA header*

Description

Extract transcript identifier from protein FASTA header

Usage

```
prot_hdr_to_enst(h)
```

Arguments

h
: Character string giving a single FASTA header line (including the leading ‘>‘ symbol if present).

Details

GENCODE protein FASTA headers typically contain a transcript reference such as:

“‘ >ENSP00000369497.3|ENST00000355832.3|ENSG00000141510.15|... “‘

or may encode it in tagged fields like ‘transcript:ENST...‘ or ‘transcript_id=ENSMUST...‘. This function uses regular-expression pattern matching to locate the transcript identifier, strips the version suffix (e.g. ‘.3‘), and returns the cleaned transcript ID.

Value

A character string containing the transcript identifier (without version suffix). Returns an empty string if no match is found.

---

restrict_gtf_genetype *Restrict GTF entries by gene type (internal)*

Description

Internal helper to subset a GTF `data.frame` or `data.table` to include only selected gene biotypes (e.g. protein_coding, lncRNA).

Usage

```
restrict_gtf_genetype(
  gtf_df,
  restrictions = c("protein_coding", "lncRNA", "snoRNA", "snRNA", "rRNA", "miRNA",
    "MT_tRNA", "MT_rRNA")
)
```

Arguments

`gtf_df`	A `data.frame` or `data.table` containing a `gene_type` column.
`restrictions`	Character vector of allowed `gene_type` values. Defaults to common gene biotypes.

Value

A subset of `gtf_df` containing only rows whose `gene_type` matches one of the specified `restrictions`.

---

restrict_gtf_rowtype *Restrict GTF entries by feature type (internal)*

Description

Internal helper to subset a GTF `data.frame` or `data.table` to retain only `gene`, `exon`, and `transcript` rows.

Usage

```
restrict_gtf_rowtype(gtf_df)
```

Arguments

`gtf_df`	A `data.frame` or `data.table` containing a `type` column (e.g. output of [load_gtf_long()]).

Value

A subset of `gtf_df` including only rows where `type` is one of `"gene"`, `"exon"`, or `"transcript"`.

`SpliceImpactResult-class` *SpliceImpact result container (S4)*

Description

SpliceImpact result container (S4)

Slots

`raw_events` ‘SummarizedExperiment‘ of sample/form-level rows.

`di_events` ‘GRanges‘ of differential inclusion rows.

`res_di` ‘GRanges‘ of threshold-filtered differential rows.

`matched` ‘S4Vectors::DataFrame‘ of annotation-matched DI rows.

`sample_frame` ‘S4Vectors::DataFrame‘ sample manifest (‘path‘, ‘sample_name‘, ‘condition‘) when available.

`paired_hits` ‘GRanges‘ of paired event-level rows.

`segments` ‘GRangesList‘ of per-event segment parts (‘inc_case‘, etc.).

`metadata` list with flags and optional provenance.

`spliceimpact_hit_colsets` *List predefined paired-hit column subsets*

Description

List predefined paired-hit column subsets

Usage

```
spliceimpact_hit_colsets()
```

Value

Named list of predefined column vectors for paired-hit accessors.

spliceimpact_s4_guide *Detailed guide for using SpliceImpactResult*

Description

Prints practical guidance on slots, assays, key columns, and common access patterns for conversion between S4 and ‘data.table‘.

Usage

```
spliceimpact_s4_guide(as_markdown = FALSE)
```

Arguments

as_markdown	Logical; if ‘TRUE‘, returns guide text instead of printing.

Value

Invisible character guide text (or visible text if ‘as_markdown = TRUE‘).

Examples

```
guide_txt <- spliceimpact_s4_guide(as_markdown = TRUE)
cat(substr(guide_txt, 1, 80), "\n")
```

spliceimpact_s4_schema *S4 slot and key schema for SpliceImpactResult*

Description

S4 slot and key schema for SpliceImpactResult

Usage

```
spliceimpact_s4_schema()
```

Value

Named list describing slots, core key columns, and assay names.

Examples

```
schema <- spliceimpact_s4_schema()
names(schema)
```

split_into_bits   *Split GTF transcripts into balanced chromosome groups (internal)*

Description

Internal helper that groups protein-coding transcripts by chromosome, ensuring that each group remains below a cumulative size threshold. Useful for dividing GTF processing or annotation tasks into balanced batches.

Usage

```
split_into_bits(gtf_df, max_group_size)
```

Arguments

`gtf_df`	A `data.frame` or `data.table` containing GTF annotations, typically from [load_gtf_long()].
`max_group_size`	Numeric scalar giving the maximum total number of transcripts allowed per group (passed to `bin_under_cap()`).

Details

The function considers only transcripts where `type == "transcript"`, `transcript_type == "protein_coding"`

Chromosome names are simplified by removing a leading `"chr"` prefix before grouping.

Value

A list of character vectors, where each element corresponds to a bin of chromosome names grouped under the cumulative cap.

strip_ver   *Strip version suffix from identifiers (internal)*

Description

Removes trailing version components (e.g., ".1", ".2") from Ensembl or similar identifiers.

Usage

```
strip_ver(x)
```

Arguments

`x`	Character vector of identifiers.

Value

A character vector with version suffixes removed.

to_long_features *Convert wide BioMart feature table to long format (internal)*

Description

Internal helper that reshapes a wide BioMart results table containing per-feature columns (e.g. InterPro, Pfam, TMHMM) into a unified long format suitable for downstream annotation or visualization.

Usage

```
to_long_features(
  ipr,
  features = c("mobidblite", "seg", "ncoils", "tmhmm", "signalp"),
  include_interpro = TRUE
)
```

Arguments

`ipr` A `data.frame` or `data.table` returned from [biomaRt::getBM()] containing per-transcript protein feature data.

`features` Character vector of feature prefixes to include (default: `c("mobidblite","seg","ncoils","tmhmm","s`

`include_interpro`
Logical; whether to also include InterPro annotations if present (default `TRUE`).

Details

For each feature type `x`, the function expects columns `x`, `x_start`, and `x_end`. These are combined into a single long table. Non-InterPro features use the feature ID for all name fields. InterPro entries optionally use the description fields `interpro_description` and `interpro_short_description` if available.

Value

A `data.table` in long format with columns: `ensembl_transcript_id`, `ensembl_peptide_id`, `database`, `feature_id`, `name`, `alt_name`, `start`, `stop`, and `method = "biomaRt"`.

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