

# Package ‘rtemis.a3’

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**Title** Amino Acid Annotation (A3) Format

**Version** 0.5.3

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**Description** Implements the Amino Acid Annotation (A3) format using 'S7' classes.

The A3 format is a structured schema for annotating amino acid sequences with site, region, post-translational modification (PTM), processing event, and variant information.

Provides functions to create, read, and write A3 objects, and to import annotations from 'UniProt', 'AlphaFold', 'PDBe', 'ClinVar', and 'Ensembl'.

**URL** <https://a3.rtemis.org>

**BugReports** <https://github.com/rtemis-org/a3/issues>

**License** GPL (>= 3)

**Encoding** UTF-8

**RoxygenNote** 7.3.3

**Depends** R (>= 4.1.0)

**Imports** cli, data.table, rtemis.core, S7, utils

**Suggests** biomaRt, httr, jsonlite, seqinr, testthat (>= 3.0.0)

**Config/testthat/edition** 3

**NeedsCompilation** no

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**Repository** CRAN

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rtemis.a3-package      *rtemis.a3: Amino Acid Annotation format*

---

## Description

Amino Acid Annotation format utilities

## Details

**rtemis.a3**: Amino Acid Annotation format

## Author(s)

**Maintainer:** E.D. Gennatas <gennatas@gmail.com> ([ORCID](#)) [copyright holder]

## See Also

Useful links:

- <https://a3.rtemis.org>
- Report bugs at <https://github.com/rtemis-org/a3/issues>

---

aa\_sub                      *Perform amino acid substitutions*

---

**Description**

Perform amino acid substitutions

**Usage**

```
aa_sub(x, substitutions, verbosity = 1L)
```

**Arguments**

x	Character vector: Amino acid sequence. e.g. "ARND" or c("A", "R", "N", "D").
substitutions	Character vector: Substitutions to perform in the format "OriginalPositionNew", e.g. c("C291A", "C322A").
verbosity	Integer: Verbosity level.

**Value**

Character vector with substitutions performed.

**Author(s)**

EDG

**Examples**

```
aa_sub(c("A", "R", "N", "D"), c("R2K", "N3S"))
```

---

annotation\_position      *Create position-based annotations for A3*

---

**Description**

Creates an annotation spec (named list) with an A3Position index and optional type, for use with create\_A3().

**Usage**

```
annotation_position(x, type = NULL)
```

**Arguments**

x	Integer vector: Positions of the annotation (1-based indexing).
type	Optional character scalar: Annotation type. NULL is treated as the empty string in the canonical A3 representation.

**Value**

Named list with index (A3Position) and type (character)

**Author(s)**

EDG

**Examples**

```
# Create a site annotation for positions 5 and 17, of type "active site"
annotation_position(c(5L, 17L), type = "active site")
```

---

annotation\_range      *Create range-based annotations for A3*

---

**Description**

Creates an annotation spec (named list) with an A3Range index and optional type, for use with create\_A3().

**Usage**

```
annotation_range(x, type = NULL)
```

**Arguments**

x	Integer matrix with 2 columns corresponding to start and end positions of the annotation (1-based indexing).
type	Optional character scalar: Annotation type. NULL is treated as the empty string in the canonical A3 representation.

**Value**

Named list with index (A3Range) and type (character)

**Author(s)**

EDG

**Examples**

```
# Create a region annotation for ranges 3-10 and 15-22, of type "repeat"
annotation_range(rbind(c(3L, 10L), c(15L, 22L)), type = "repeat")
```

---

annotation\_variant      *Create variant annotations for A3*

---

### Description

Creates an A3Variant object for variant annotations with position and info.

### Usage

```
annotation_variant(x, info = list())
```

### Arguments

x	Integer scalar: Position of the variant (1-based indexing).
info	Named list: Additional information about the variant (e.g. reference and alternate amino acids, variant type, etc.)

### Value

A3Variant object

### Author(s)

EDG

### Examples

```
# Create a variant annotation for position 10 with info about the variant
annotation_variant(10L, info = list(ref = "A", alt = "T", type = "missense"))
```

---

clinvar\_variants      *Fetch ClinVar variants for a gene and parse them into A3Variant objects*

---

### Description

Queries the NCBI ClinVar database via E-utilities for all variants associated with a gene, and returns those with protein-level amino acid changes as a named list of A3Variant objects.

**Usage**

```
clinvar_variants(
  gene,
  significance = c("pathogenic", "likely_pathogenic"),
  max_variants = 500L,
  esearch_url = "https://eutils.ncbi.nlm.nih.gov/entrez/eutils/esearch.fcgi",
  esummary_url = "https://eutils.ncbi.nlm.nih.gov/entrez/eutils/esummary.fcgi",
  batch_size = 500L,
  verbosity = 1L
)
```

**Arguments**

gene	Character scalar: HGNC gene symbol, e.g. "MAPT".
significance	Character vector: Clinical significance filter. Any combination of "pathogenic", "likely_pathogenic", "uncertain_significance", "likely_benign", "benign". Pass NULL to fetch all records regardless of significance.
max_variants	Integer scalar: Maximum number of ClinVar records to fetch after filtering. Defaults to 500L.
esearch_url	Character scalar: NCBI E-utilities esearch endpoint.
esummary_url	Character scalar: NCBI E-utilities esummary endpoint.
batch_size	Integer scalar: Number of UIDs per esummary request. NCBI recommends no more than 500 per request.
verbosity	Integer scalar: Verbosity level.

**Details**

Variants without a parseable protein change (intronic, regulatory, etc.) are silently skipped.

**Value**

Named list of A3Variant objects. Names use {from}{position}{to} notation (e.g. "R406W"), with a numeric suffix to disambiguate duplicates.

**Author(s)**

EDG

**Examples**

```
# Requires internet connection and fetches data from ClinVar.
## Not run:
# Pathogenic and likely pathogenic variants (default)
mapt_variants <- clinvar_variants("MAPT")
# All variants regardless of significance
mapt_all <- clinvar_variants("MAPT", significance = NULL)

## End(Not run)
```

---

concat	<i>Concatenate character vector to single string for sequence input</i>
--------	---

---

**Description**

Concatenate character vector to single string for sequence input

**Usage**

```
concat(x)
```

**Arguments**

x                      Character vector to concatenate

**Value**

Single character string

**Author(s)**

EDG

**Examples**

```
# Concatenate a character vector of single-letter amino acids into a sequence string
concat(c("M", "A", "E", "P", "R"))
```

---

create_A3	<i>Create an A3 object from sequence, annotations, and metadata</i>
-----------	---

---

**Description**

Create an A3 object from sequence, annotations, and metadata

**Usage**

```
create_A3(
  sequence,
  site = list(),
  region = list(),
  ptm = list(),
  processing = list(),
  variant = list(),
  uniprot_id = NULL,
  description = NULL,
```

```

    reference = NULL,
    organism = NULL
  )

```

### Arguments

sequence	Character scalar: Amino acid sequence string.
site	Named list of site annotations
region	Named list of region annotations
ptm	Named list of PTM annotations
processing	Named list of processing annotations
variant	Named list of variant annotations
uniprot_id	Optional character scalar: UniProt accession.
description	Optional character scalar: Protein description.
reference	Optional character scalar: Citation or URL.
organism	Optional character scalar: Species name.

### Value

A3 object

### Author(s)

EDG

### Examples

```

# Minimal: sequence only
a <- create_A3("MAEPRQEFVEMDHAGTYGLGDRK")

# With site, region, and PTM annotations
a <- create_A3(
  "MAEPRQEFVEMDHAGTYGLGDRK",
  site = list(
    Active_site = annotation_position(c(5L, 17L), type = "active site")
  ),
  region = list(
    Domain = annotation_range(rbind(c(3L, 10L), c(15L, 22L)),
      type = "repeat"
    )
  ),
  ptm = list(
    Phosphorylation = annotation_position(c(2L, 18L), type = "phosphoserine")
  ),
  uniprot_id = "P10636",
  organism = "Homo sapiens"
)

```

---

gene2sequence	<i>Get the coding sequence of a gene</i>
---------------	--

---

**Description**

Get the coding sequence of a gene

**Usage**

```
gene2sequence(  
  gene,  
  organism = "hsapiens",  
  biomaRt = "ensembl",  
  host = "https://www.ensembl.org",  
  verbosity = 1L  
)
```

**Arguments**

gene	Character vector: One or more HGNC gene symbols.
organism	Character scalar: Organism short name (Ensembl convention, e.g. "hsapiens").
biomaRt	Character scalar: BioMart name.
host	Character scalar: Host address.
verbosity	Integer: Verbosity level.

**Value**

data.frame with columns "gene", "ensembl\_transcript\_id" and "sequence".

**Author(s)**

EDG

**Examples**

```
# Requires internet connection and fetches data from Ensembl using biomaRt.  
## Not run:  
  mapt_seq <- gene2sequence("MAPT")  
  
## End(Not run)
```

---

get\_alphafold                    *Get AlphaFold info for a given UniProt ID*

---

**Description**

Get AlphaFold info for a given UniProt ID

**Usage**

```
get_alphafold(uniprotid)
```

**Arguments**

uniprotid            Character: UniProt ID.

**Value**

data frame with AlphaFold info.

**Author(s)**

EDG

**Examples**

```
# Requires internet connection and fetches data from AlphaFold.
## Not run:
get_alphafold("P10636")

## End(Not run)
```

---

pdb\_annotations                    *Fetch PDB structural annotations for a UniProt accession*

---

**Description**

Queries the PDBe APIs for secondary structure and ligand binding sites from experimental PDB structures, converts residue numbers to UniProt canonical coordinates via SIFTS, and returns named lists of A3Region and A3Site objects ready for use with create\_A3().

**Usage**

```
pdb_annotations(
  accession,
  pdb_id = NULL,
  pdbe_graph_url = "https://www.ebi.ac.uk/pdbe/graph-api",
  pdbe_api_url = "https://www.ebi.ac.uk/pdbe/api",
  verbosity = 1L
)
```

**Arguments**

accession	Character scalar: UniProt accession, e.g. "P10636".
pdb_id	Optional character scalar: Four-character PDB ID (e.g. "2mz7"). If NULL, the top-ranked structure from PDBe is used.
pdbe_graph_url	Character scalar: PDBe Graph API base URL.
pdbe_api_url	Character scalar: PDBe REST API base URL.
verbosity	Integer scalar: Verbosity level.

**Details**

Structure ranking and SIFTS residue mappings come from the PDBe Graph API best\_structures endpoint. Secondary structure and binding sites are fetched from the PDBe REST API.

When `pdb_id` is NULL the top-ranked structure (by PDBe coverage score) is used automatically.

**Value**

Named list with two elements:

`region` Named list of A3Region objects for secondary structure (types: "helix", "betaStrand", "turn").

`site` Named list of A3Site objects for ligand binding sites (type: "bindingSite").

**Author(s)**

EDG

**Examples**

```
# Requires internet connection and fetches data from PDBe.
## Not run:
ann <- pdb_annotations("P10636")
mapt <- create_A3(
  sequence = uniprot_sequence("P10636"),
  region   = ann[["region"]],
  site     = ann[["site"]]
)

## End(Not run)
```

---

read\_A3json                      *Read A3 object from JSON file*

---

**Description**

Read A3 object from JSON file

**Usage**

```
read_A3json(filepath, verbosity = 1L)
```

**Arguments**

filepath                      Character: Path to JSON file.  
verbosity                    Integer: if greater than 0, print messages.

**Value**

A3 object.

**Author(s)**

EDG

**Examples**

```
a3 <- create_A3("MAEPRQEFVEMDHAGTYGLGDRK", uniprot_id = "P10636")  
tmp <- tempfile(fileext = ".json")  
write_A3json(a3, tmp)  
a3_read <- read_A3json(tmp, verbosity = 0L)  
unlink(tmp)
```

---

uniprot\_sequence                *Fetch a protein sequence from UniProt*

---

**Description**

Lightweight FASTA-only fetch. Use this when you only need the amino acid sequence. For full annotations and metadata use [uniprot\\_to\\_A3\(\)](#).

**Usage**

```
uniprot_sequence(  
  accession,  
  base_url = "https://rest.uniprot.org/uniprotkb",  
  verbosity = 1L  
)
```

**Arguments**

accession	Character scalar: UniProt accession, e.g. "P10636".
base_url	Character scalar: UniProt REST API base URL.
verbosity	Integer scalar: Verbosity level.

**Value**

Character scalar: amino acid sequence in single-letter code.

**Author(s)**

EDG

**Examples**

```
# Requires internet connection and fetches data from UniProt.
## Not run:
seq <- uniprot_sequence("P10636")

## End(Not run)
```

---

uniprot\_to\_A3

---

*Fetch a UniProt entry and parse it into an A3 object*


---

**Description**

Fetches the UniProt JSON for the given accession via the UniProt REST API, maps all sequence annotations to the A3 schema (see specs/uniprot.md), and returns a fully populated A3 object.

**Usage**

```
uniprot_to_A3(
  accession,
  base_url = "https://rest.uniprot.org/uniprotkb",
  verbosity = 1L
)
```

**Arguments**

accession	Character scalar: UniProt accession, e.g. "P10636".
base_url	Character scalar: UniProt REST API base URL.
verbosity	Integer scalar: Verbosity level.

**Details**

Feature types not mapped to A3 (mutagenesis, alternative sequences, sequence conflicts, etc.) are silently ignored.

**Value**

A3 object with sequence, annotations, and UniProt metadata.

**Author(s)**

EDG

**Examples**

```
# Requires internet connection and fetches data from UniProt.
## Not run:
mapt <- uniprot_to_A3("P10636")

## End(Not run)
```

---

write_A3json	<i>Write A3 object to JSON file</i>
--------------	-------------------------------------

---

**Description**

Write A3 object to JSON file

**Usage**

```
write_A3json(x, filepath, overwrite = FALSE)
```

**Arguments**

x	A3 object.
filepath	Character: Path to save JSON file.
overwrite	Logical: If TRUE, overwrite existing file.

**Value**

Invisible x. Writes JSON file as side effect.

**Author(s)**

EDG

**Examples**

```
a3 <- create_A3("MAEPRQEFVEMDHAGTYGLGDRK", uniprot_id = "P10636")
tmp <- tempfile(fileext = ".json")
write_A3json(a3, tmp)
a3_read <- read_A3json(tmp)
unlink(tmp)
```

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