

Using Bioconductor's Annotation Libraries

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Overview

The Bioconductor project maintains a rich body of annotation data assembled into R libraries. The purpose of this vignette is to discuss the structure, contents, and usage of these annotation data libraries. Executable code is provided as examples.

Contents

Bioconductor's annotation data libraries are constructed by assembling data collected from various public data repositories using Bioconductor's *AnnotationDbi* package and distributed as regular R libraries that can be installed and loaded in the same way an R library is installed/loaded. Each annotation library is an independent unit that can be used alone or in conjunction with other annotation libraries. Platform specific libraries are a group annotation libraries assembled specifically for given platforms (e. g. Affymetrix HG_U95Av2). `org.XX.eg.db` are libraries containing data assembled at genome level for specific organisms such as human, mouse, fly, or rat. *KEGG.db* and *GO.db* are source specific libraries containing generic data for various genomes.

Each annotation library, when installed, contains a sqlite database contained within the `extdata` along with a `man` subdirectory filled with documentation about the data. The data can be accessed using the standard methods that would work for the classic environment objects (hash table with key-value pairs) and act as if they were simple associations of annotation values to a set of keys. For each of these emulated environment objects (which we will refer to as mappings), there is a corresponding help file in the `man` directory with detail descriptions of the data file and usage. In addition to the traditional access to these data, these databases can also be accessed directly by using DBI interfaces which allow for powerful new combinations of these data.

Each platform specific library creates a series of these mapping objects named by following the convention of package name plus mapping name. The package name is in lower case letters and the mapping names are in capital letters. When a given mapping maps platform specific keys to annotation data, only the name of the annotation data is used for the name of the mapping. Otherwise, the mapping names have a pattern of key name and value name joined by a "2" in between. For example, `hgu95av2ENTREZID` maps probe ids on an Affymetrix human genome U95Av2 chip to EntrezGene IDs while `hgu95av2GO2PROBE` maps Gene Ontology IDs to probe IDs. Names of the mappings available in a platform specific data package are not listed here to save space but are easily accessible as shown later in the section for usage.

Genome level annotation libraries are named in the form of `org.Xx.yy.db` where `Xx` represents an abbreviation of the genus and species. Each of the organism wide genome annotation packages is based upon some type of widely used gene based identifier (such as an Entrez Gene id) that is mapped onto all the other features in the package. The `yy` part of the name corresponds to this designation, where `eg` means a package is an entrez gene package and `sgd` is a package based on the `sgd` database etc. In many cases the `org` packages will contain more different kinds of information than the platform based ones, since not all types of information are as widely sought after.

The *KEGG.db* library contains mappings between ids such as Entrez Gene IDs and *GO* to *KEGG* pathway ids and thus also to pathway names. The *GO.db* library maintain the directed acyclic graph structure of the original data from Gene Ontology Consortium by providing mappings of *GO* ids to their direct parents or children for each of the three categories (molecular function, cellular component, and biological process). Mappings between Entrez Gene and *GO* ids are also available to complement the *GO.db* package. These mappings are found within the organism wide packages mentioned above. These mappings are provided with evidence code that specifies the type of evidence that supports the annotation of a gene to a particular *GO* term.

Usage

All the annotation libraries can be obtained from the Bioconductor web site (<http://www.bioconductor.org>). To illustrate their usages, we use the library for Affymetrix HG_U95Av2 chip (*hgu95av2.db*) as an example for platform specific data packages and the *GO.db* library for non-platform specific data packages. We assume that R (www.r-project.org) and Bioconductor's Biobase and annotation libraries have already been installed.

Package installation

Download libraries *hgu95av2.db* and *GO.db* with `BiocManager::install()`. If the *reposTools* library has already been installed/loaded, typing `install.packages2(library name)` installs the library for both Unix and Windows.

Typing `library(library name)` in an R session will load the library into R. For example,

```
> library("annotate")
> library("hgu95av2.db")
> library("GO.db")
```

Documentations

Each library contains documentation for the library in general and each of the individual mapping objects contained by the library. Two documents at the library level can be accessed by typing a library basename preceded by a question mark (e. g. `?hgu95av2`) and the library basename followed by a pair of brackets (e. g. `hgu95av2()`), respectively. The former explains what the package is and details how a user can get more

information, while the latter lists all the mappings contained by a library and provides information on the total number of keys within each of the maps contained by the library and how many of these keys are annotated. In addition, the latter will indicate the sources for the information provided by the package as well as the date that these sources claim to have last been updated.

The documentation for a given mapping object can be accessed by typing the name of an mapping object proceeded by a question mark (e. g. `hgu95av2GO`). The resulting documentation provides detail explanations to the mapping object, data source used to build the object, and example code for accessing annotation data.

Accessing annotation data within a library

Annotation data of a given library are stored as mapping objects in the form of key (items to be annotated) and value (annotation for an key item) pairs. Each mapping object provides annotation for keys for a particular subject reflected by the name of the object. For example, `hgu95av2GO` annotates probes on the HGU95Av2 chip with ids of the Gene Ontology terms the probes correspond to.

The name of an mapping object consists of package basename (*hgu95av2.db*) and mapping name (*GO*) to avoid confusion when multiple libraries are loaded to the system at the same time. Data contained by an mapping can be accessed easily using Bioconductor's existing functions. For example, the following code stores all the keys contained by the `hgu95av2GO` mapping object to variable *temp* and displays the first five keys on the screen:

```
> as.list(hgu95av2GO[5])

$`1004_at`
$`1004_at`$`GO:0006955`
$`1004_at`$`GO:0006955`$GOID
[1] "GO:0006955"

$`1004_at`$`GO:0006955`$Evidence
[1] "IBA"

$`1004_at`$`GO:0006955`$Ontology
[1] "BP"

$`1004_at`$`GO:0007186`
$`1004_at`$`GO:0007186`$GOID
[1] "GO:0007186"

$`1004_at`$`GO:0007186`$Evidence
[1] "IEA"

$`1004_at`$`GO:0007186`$Ontology
```

[1] "BP"

```
$`1004_at`$`GO:0007204`  
$`1004_at`$`GO:0007204`$GOID  
[1] "GO:0007204"
```

```
$`1004_at`$`GO:0007204`$Evidence  
[1] "IBA"
```

```
$`1004_at`$`GO:0007204`$Ontology  
[1] "BP"
```

```
$`1004_at`$`GO:0019722`  
$`1004_at`$`GO:0019722`$GOID  
[1] "GO:0019722"
```

```
$`1004_at`$`GO:0019722`$Evidence  
[1] "IBA"
```

```
$`1004_at`$`GO:0019722`$Ontology  
[1] "BP"
```

```
$`1004_at`$`GO:0030595`  
$`1004_at`$`GO:0030595`$GOID  
[1] "GO:0030595"
```

```
$`1004_at`$`GO:0030595`$Evidence  
[1] "IEA"
```

```
$`1004_at`$`GO:0030595`$Ontology  
[1] "BP"
```

```
$`1004_at`$`GO:0032467`  
$`1004_at`$`GO:0032467`$GOID  
[1] "GO:0032467"
```

```
$`1004_at`$`GO:0032467`$Evidence  
[1] "IMP"
```

```
$`1004_at`$`GO:0032467`$Ontology  
[1] "BP"
```

```

$`1004_at`$`GO:0042113`
$`1004_at`$`GO:0042113`$GOID
[1] "GO:0042113"

$`1004_at`$`GO:0042113`$Evidence
[1] "IEA"

$`1004_at`$`GO:0042113`$Ontology
[1] "BP"

$`1004_at`$`GO:0048535`
$`1004_at`$`GO:0048535`$GOID
[1] "GO:0048535"

$`1004_at`$`GO:0048535`$Evidence
[1] "IEA"

$`1004_at`$`GO:0048535`$Ontology
[1] "BP"

$`1004_at`$`GO:0060326`
$`1004_at`$`GO:0060326`$GOID
[1] "GO:0060326"

$`1004_at`$`GO:0060326`$Evidence
[1] "IBA"

$`1004_at`$`GO:0060326`$Ontology
[1] "BP"

$`1004_at`$`GO:0070098`
$`1004_at`$`GO:0070098`$GOID
[1] "GO:0070098"

$`1004_at`$`GO:0070098`$Evidence
[1] "IEA"

$`1004_at`$`GO:0070098`$Ontology
[1] "BP"

$`1004_at`$`GO:0005886`

```

```

$`1004_at`$`GO:0005886`$GOID
[1] "GO:0005886"

$`1004_at`$`GO:0005886`$Evidence
[1] "TAS"

$`1004_at`$`GO:0005886`$Ontology
[1] "CC"


$`1004_at`$`GO:0009897`
$`1004_at`$`GO:0009897`$GOID
[1] "GO:0009897"

$`1004_at`$`GO:0009897`$Evidence
[1] "IBA"

$`1004_at`$`GO:0009897`$Ontology
[1] "CC"


$`1004_at`$`GO:0004930`
$`1004_at`$`GO:0004930`$GOID
[1] "GO:0004930"

$`1004_at`$`GO:0004930`$Evidence
[1] "TAS"

$`1004_at`$`GO:0004930`$Ontology
[1] "MF"


$`1004_at`$`GO:0005515`
$`1004_at`$`GO:0005515`$GOID
[1] "GO:0005515"

$`1004_at`$`GO:0005515`$Evidence
[1] "IPI"

$`1004_at`$`GO:0005515`$Ontology
[1] "MF"


$`1004_at`$`GO:0016493`
$`1004_at`$`GO:0016493`$GOID
[1] "GO:0016493"

```

```
$`1004_at`$`GO:0016493`$Evidence
```

```
[1] "IBA"
```

```
$`1004_at`$`GO:0016493`$Ontology
```

```
[1] "MF"
```

```
$`1004_at`$`GO:0016494`
```

```
$`1004_at`$`GO:0016494`$GOID
```

```
[1] "GO:0016494"
```

```
$`1004_at`$`GO:0016494`$Evidence
```

```
[1] "IEA"
```

```
$`1004_at`$`GO:0016494`$Ontology
```

```
[1] "MF"
```

```
$`1004_at`$`GO:0019957`
```

```
$`1004_at`$`GO:0019957`$GOID
```

```
[1] "GO:0019957"
```

```
$`1004_at`$`GO:0019957`$Evidence
```

```
[1] "IBA"
```

```
$`1004_at`$`GO:0019957`$Ontology
```

```
[1] "MF"
```

To obtain annotation for a given set of keys, one may use the `mget` function. Suppose we have run an experiment using the HG_U95Av2 chip and found three genes represented by Affymetrix probe ids *738_at*, *40840_at*, and *41668_r_at* interesting. To get the names of genes the three probe ids corresponding to, we do:

```
> mget(c("738_at", "40840_at", "41668_r_at"), hgu95av2GENENAME)
```

```
$`738_at`
```

```
[1] "5'-nucleotidase, cytosolic II"
```

```
$`40840_at`
```

```
[1] "peptidylprolyl isomerase F"
```

```
$`41668_r_at`
```

```
[1] "TDP-glucose 4,6-dehydratase"
```

Similarly, identifiers of Gene Ontology terms corresponding to the three probes can be obtained as shown below:

```
> temp <- mget(c("41561_s_at", "40840_at", "41668_r_at"), hgu95av2GO)
```

In this case, the function `mget` returns a list of pre-defined S4 objects containing data for the ids, ontology, and evidence code of Gene Ontology terms corresponding to the three keys. The following code shows how to access the GO id, evidence code and ontology of the Gene Ontology term corresponding to probe id `40840_at`:

```
> temp <- get("738_at", hgu95av2GO)
> names(temp)

[1] "GO:0000255" "GO:0006204" "GO:0046037" "GO:0046040" "GO:0046040"
[6] "GO:0046054" "GO:0046085" "GO:0050689" "GO:0005737" "GO:0005829"
[11] "GO:0005829" "GO:0005515" "GO:0005524" "GO:0008253" "GO:0008253"
[16] "GO:0008253" "GO:0042802" "GO:0046872" "GO:0050146" "GO:0050483"
[21] "GO:0050484" "GO:0061630" "GO:0106411"

> temp[["GO:0008253"]][["Evidence"]]

[1] "IBA"

> temp[["GO:0008253"]][["Ontology"]]

[1] "MF"
```

As shown above, probe `40840_at` can be annotated by three Gene Ontology terms identified by `GO:0005829`, `GO:0008253`, and `GO:0016787`. The evidence code for `GO:0008253` is *TAS* (traceable author statement) and it belongs to ontology *MF* (molecular function).

Accessing annotation data across libraries

Often, data available in a given data package alone may not be sufficient and need to be sought across packages. Bioconductor's annotation data packages are linked by common public data identifiers to allow traverse between packages (Fig. 1). Using the example above, we know that probe id `738_at` are annotated by three Gene Ontology ids `GO:0005829`, `GO:0008253`, and `GO:0016787`. The Gene Ontology terms for various Gene Ontology ids, however, are stored in another package named *GO.db*. AS package *hgu95av2.db* and *GO.db* are linked by *GO* ids, one can annotate probe id `738_at` with Gene Ontology terms by linking data in the two packages using *GO* id as shown below:

```
> mget(names(get("738_at", hgu95av2GO)), GOTERM)

$`GO:0000255`
GOID: GO:0000255
Term: allantoin metabolic process
Ontology: BP
Definition: The chemical reactions and pathways involving
```


allantoin, (2,5-dioxo-4-imidazolidinyl)urea, an
intermediate or end product of purine catabolism.
Synonym: allantoin metabolism

\$`GO:0006204`
GOID: GO:0006204
Term: IMP catabolic process
Ontology: BP
Definition: The chemical reactions and pathways resulting in
the breakdown of IMP, inosine monophosphate.
Synonym: IMP breakdown
Synonym: IMP catabolism
Synonym: IMP degradation

\$`GO:0046037`
GOID: GO:0046037
Term: GMP metabolic process
Ontology: BP
Definition: The chemical reactions and pathways involving GMP,
guanosine monophosphate.
Synonym: GMP metabolism

\$`GO:0046040`
GOID: GO:0046040
Term: IMP metabolic process
Ontology: BP
Definition: The chemical reactions and pathways involving IMP,
inosine monophosphate.
Synonym: IMP metabolism

\$`GO:0046040`
GOID: GO:0046040
Term: IMP metabolic process
Ontology: BP
Definition: The chemical reactions and pathways involving IMP,
inosine monophosphate.
Synonym: IMP metabolism

\$`GO:0046054`
GOID: GO:0046054
Term: dGMP metabolic process
Ontology: BP
Definition: The chemical reactions and pathways involving
dGMP, deoxyguanosine monophosphate (2'-deoxyguanosine
5'-phosphate).
Synonym: dGMP metabolism

\$`GO:0046085`
GOID: GO:0046085
Term: adenosine metabolic process
Ontology: BP
Definition: The chemical reactions and pathways involving adenosine, adenine riboside, a ribonucleoside found widely distributed in cells of every type as the free nucleoside and in combination in nucleic acids and various nucleoside coenzymes.
Synonym: adenosine metabolism

\$`GO:0050689`
GOID: GO:0050689
Term: negative regulation of defense response to virus by host
Ontology: BP
Definition: Any host process that results in the inhibition of antiviral immune response mechanisms, thereby facilitating viral replication. The host is defined as the larger of the organisms involved in a symbiotic interaction.
Synonym: down regulation of antiviral response by host
Synonym: down-regulation of antiviral response by host
Synonym: downregulation of antiviral response by host
Synonym: negative regulation by host of antiviral response
Synonym: negative regulation of antiviral response by host
Synonym: inhibition of antiviral response by host

\$`GO:0005737`
GOID: GO:0005737
Term: cytoplasm
Ontology: CC
Definition: The contents of a cell excluding the plasma membrane and nucleus, but including other subcellular structures.

\$`GO:0005829`
GOID: GO:0005829
Term: cytosol
Ontology: CC
Definition: The part of the cytoplasm that does not contain organelles but which does contain other particulate matter, such as protein complexes.

\$`GO:0005829`
GOID: GO:0005829
Term: cytosol

Ontology: CC
Definition: The part of the cytoplasm that does not contain
organelles but which does contain other particulate
matter, such as protein complexes.

\$`GO:0005515`
GOID: GO:0005515
Term: protein binding
Ontology: MF
Definition: Binding to a protein.
Synonym: GO:0001948
Synonym: GO:0045308
Synonym: protein amino acid binding
Synonym: glycoprotein binding
Secondary: GO:0001948
Secondary: GO:0045308

\$`GO:0005524`
GOID: GO:0005524
Term: ATP binding
Ontology: MF
Definition: Binding to ATP, adenosine 5'-triphosphate, a
universally important coenzyme and enzyme regulator.
Synonym: Mg-ATP binding
Synonym: MgATP binding

\$`GO:0008253`
GOID: GO:0008253
Term: 5'-nucleotidase activity
Ontology: MF
Definition: Catalysis of the reaction: a 5'-ribonucleotide +
H₂O = a ribonucleoside + phosphate.
Synonym: 5' nucleotidase activity
Synonym: 5'-mononucleotidase activity
Synonym: 5'-ribonucleotide phosphohydrolase activity
Synonym: 5'-adenylic phosphatase
Synonym: 5'-AMP nucleotidase
Synonym: 5'-AMPase
Synonym: adenosine 5'-phosphatase
Synonym: adenosine monophosphatase
Synonym: AMP phosphatase
Synonym: AMP phosphohydrolase
Synonym: AMPase
Synonym: snake venom 5'-nucleotidase
Synonym: thimidine monophosphate nucleotidase
Synonym: UMPase

Synonym: uridine 5'-nucleotidase

\$`GO:0008253`

GOID: GO:0008253

Term: 5'-nucleotidase activity

Ontology: MF

Definition: Catalysis of the reaction: a 5'-ribonucleotide +
H₂O = a ribonucleoside + phosphate.

Synonym: 5' nucleotidase activity

Synonym: 5'-mononucleotidase activity

Synonym: 5'-ribonucleotide phosphohydrolase activity

Synonym: 5'-adenylic phosphatase

Synonym: 5'-AMP nucleotidase

Synonym: 5'-AMPase

Synonym: adenosine 5'-phosphatase

Synonym: adenosine monophosphatase

Synonym: AMP phosphatase

Synonym: AMP phosphohydrolase

Synonym: AMPase

Synonym: snake venom 5'-nucleotidase

Synonym: thimidine monophosphate nucleotidase

Synonym: UMPase

Synonym: uridine 5'-nucleotidase

\$`GO:0008253`

GOID: GO:0008253

Term: 5'-nucleotidase activity

Ontology: MF

Definition: Catalysis of the reaction: a 5'-ribonucleotide +
H₂O = a ribonucleoside + phosphate.

Synonym: 5' nucleotidase activity

Synonym: 5'-mononucleotidase activity

Synonym: 5'-ribonucleotide phosphohydrolase activity

Synonym: 5'-adenylic phosphatase

Synonym: 5'-AMP nucleotidase

Synonym: 5'-AMPase

Synonym: adenosine 5'-phosphatase

Synonym: adenosine monophosphatase

Synonym: AMP phosphatase

Synonym: AMP phosphohydrolase

Synonym: AMPase

Synonym: snake venom 5'-nucleotidase

Synonym: thimidine monophosphate nucleotidase

Synonym: UMPase

Synonym: uridine 5'-nucleotidase

\$`GO:0042802`
 GOID: GO:0042802
 Term: identical protein binding
 Ontology: MF
 Definition: Binding to an identical protein or proteins.
 Synonym: isoform-specific homophilic binding
 Synonym: protein homopolymerization

\$`GO:0046872`
 GOID: GO:0046872
 Term: metal ion binding
 Ontology: MF
 Definition: Binding to a metal ion.
 Synonym: metal binding
 Synonym: heavy metal binding

\$`GO:0050146`
 GOID: GO:0050146
 Term: nucleoside phosphotransferase activity
 Ontology: MF
 Definition: Catalysis of the reaction: a nucleotide + a
 2'-deoxynucleoside = a nucleoside + a 2'-deoxynucleoside
 5'-monophosphate.
 Synonym: nonspecific nucleoside phosphotransferase activity
 Synonym: nucleotide:2'-nucleoside 5'-phosphotransferase
 activity
 Synonym: nucleotide:3'-deoxynucleoside 5'-phosphotransferase
 activity
 Synonym: nucleotide:nucleoside 5'-phosphotransferase activity

\$`GO:0050483`
 GOID: GO:0050483
 Term: IMP 5'-nucleotidase activity
 Ontology: MF
 Definition: Catalysis of the reaction: 5'-IMP + H2O = inosine
 + phosphate.
 Synonym: IMP 5' nucleotidase activity
 Synonym: IMP-GMP specific 5'-nucleotidase activity

\$`GO:0050484`
 GOID: GO:0050484
 Term: GMP 5'-nucleotidase activity
 Ontology: MF
 Definition: Catalysis of the reaction: 5'-GMP + H2O =
 guanosine + phosphate.
 Synonym: GMP 5' nucleotidase activity

Synonym: IMP-GMP specific 5'-nucleotidase activity

\$`GO:0061630`

GOID: GO:0061630

Term: ubiquitin protein ligase activity

Ontology: MF

Definition: Catalysis of the transfer of ubiquitin to a substrate protein via the reaction X-ubiquitin + S = X + S-ubiquitin, where X is either an E2 or E3 enzyme, the X-ubiquitin linkage is a thioester bond, and the S-ubiquitin linkage is an amide bond: an isopeptide bond between the C-terminal glycine of ubiquitin and the epsilon-amino group of lysine residues in the substrate or, in the linear extension of ubiquitin chains, a peptide bond between the C-terminal glycine and N-terminal methionine of ubiquitin residues.

Synonym: GO:0090302

Synonym: GO:0090622

Synonym: GO:1904264

Synonym: GO:1904822

Synonym: protein ubiquitination activity

Synonym: ubiquitin ligase activity

Synonym: ER-associated E3 ligase

Synonym: E3

Secondary: GO:0090302

Secondary: GO:0090622

Secondary: GO:1904264

Secondary: GO:1904822

\$`GO:0106411`

GOID: GO:0106411

Term: XMP 5'-nucleosidase activity

Ontology: MF

Definition: Catalysis of the reaction: 5'XMP + H2O = phosphate + xanthosine.

It turns out that probe id 738_at (corresponding to *GO:0008253*, and *GO:0016787*) has molecular function (MF) *5'-nucleotidase activity* and *hydrolase activity*.

1 Session Information

The version number of R and packages loaded for generating the vignette were:

R version 4.3.1 (2023-06-16 ucrt)

Platform: x86_64-w64-mingw32/x64 (64-bit)

Running under: Windows Server 2022 x64 (build 20348)

Matrix products: default

locale:

```
[1] LC_COLLATE=C
[2] LC_CTYPE=English_United States.utf8
[3] LC_MONETARY=English_United States.utf8
[4] LC_NUMERIC=C
[5] LC_TIME=English_United States.utf8
```

time zone: America/New_York

tzcode source: internal

attached base packages:

```
[1] grid      stats4      stats      graphics  grDevices  utils
[7] datasets  methods  base
```

other attached packages:

```
[1] GO.db_3.18.0          hgu95av2.db_3.13.0    org.Hs.eg.db_3.18.0
[4] Rgraphviz_2.46.0      graph_1.80.0          xtable_1.8-4
[7] annotate_1.80.0        XML_3.99-0.14          AnnotationDbi_1.64.0
[10] IRanges_2.36.0        S4Vectors_0.40.1      Biobase_2.62.0
[13] BiocGenerics_0.48.0
```

loaded via a namespace (and not attached):

```
[1] crayon_1.5.2          vctrs_0.6.4
[3] httr_1.4.7            cli_3.6.1
[5] rlang_1.1.1           DBI_1.1.3
[7] png_0.1-8             bit_4.0.5
[9] RCurl_1.98-1.12       Biostrings_2.70.1
[11] KEGGREST_1.42.0       bitops_1.0-7
[13] fastmap_1.1.1         GenomeInfoDb_1.38.0
[15] memoise_2.0.1         compiler_4.3.1
[17] RSQLite_2.3.1         blob_1.2.4
[19] pkgconfig_2.0.3       XVector_0.42.0
[21] R6_2.5.1              GenomeInfoDbData_1.2.11
[23] tools_4.3.1           bit64_4.0.5
[25] zlibbioc_1.48.0       cachem_1.0.8
```