

# 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](http://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:0005887`
$`1004_at`$`GO:0005887`$GOID
[1] "GO:0005887"

$`1004_at`$`GO:0005887`$Evidence
[1] "TAS"

$`1004_at`$`GO:0005887`$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] "IFI"
```

```
$`1004_at`$`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:0016311" "GO:0046040" "GO:0046085"
[6] "GO:0005829" "GO:0005829" "GO:0000166" "GO:0005515" "GO:0008253"
[11] "GO:0008253" "GO:0046872" "GO:0050483"

> 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:0016311`

GOID: GO:0016311

Term: dephosphorylation

Ontology: BP

Definition: The process of removing one or more phosphoric  
(ester or anhydride) residues from a molecule.

\$`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: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: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:0000166`  
GOID: GO:0000166  
Term: nucleotide binding  
Ontology: MF  
Definition: Binding to a nucleotide, any compound consisting  
          of a nucleoside that is esterified with (ortho)phosphate  
          or an oligophosphate at any hydroxyl group on the ribose  
          or deoxyribose.

\$`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: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:0046872`

GOID: GO:0046872

Term: metal ion binding

Ontology: MF

Definition: Binding to a metal ion.

Synonym: metal binding

Synonym: heavy metal binding

\$`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

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 4.2.1 (2022-06-23)  
 Platform: aarch64-apple-darwin20 (64-bit)  
 Running under: macOS Ventura 13.0

Matrix products: default

BLAS: /Library/Frameworks/R.framework/Versions/4.2-arm64/Resources/lib/libRblas.  
 LAPACK: /Library/Frameworks/R.framework/Versions/4.2-arm64/Resources/lib/libRlapack.

locale:

[1] C/en\_US.UTF-8/en\_US.UTF-8/C/en\_US.UTF-8/en\_US.UTF-8

attached base packages:

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

other attached packages:

[1] GO.db\_3.15.0 hgu95av2.db\_3.13.0 org.Hs.eg.db\_3.15.0  
 [4] Rgraphviz\_2.42.0 graph\_1.76.0 xtable\_1.8-4  
 [7] annotate\_1.76.0 XML\_3.99-0.10 AnnotationDbi\_1.60.0  
 [10] IRanges\_2.32.0 S4Vectors\_0.36.0 Biobase\_2.58.0  
 [13] BiocGenerics\_0.44.0

loaded via a namespace (and not attached):

[1] Rcpp\_1.0.9 compiler\_4.2.1  
 [3] GenomeInfoDb\_1.34.2 XVector\_0.38.0  
 [5] bitops\_1.0-7 tools\_4.2.1  
 [7] zlibbioc\_1.44.0 bit\_4.0.4  
 [9] RSQLite\_2.2.14 memoise\_2.0.1  
 [11] pkgconfig\_2.0.3 png\_0.1-7  
 [13] rlang\_1.0.4 DBI\_1.1.3  
 [15] cli\_3.3.0 fastmap\_1.1.0  
 [17] GenomeInfoDbData\_1.2.8 httr\_1.4.3

[19]	Biostrings_2.66.0	vctrs_0.4.1
[21]	bit64_4.0.5	R6_2.5.1
[23]	blob_1.2.3	KEGGREST_1.38.0
[25]	RCurl_1.98-1.7	cachem_1.0.6
[27]	crayon_1.5.1	