

# Bioconductor: Annotation Package Overview

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## 1 Overview

In its current state the basic purpose of *annotate* is to supply interface routines that support user actions that rely on the different meta-data packages provided through the Bioconductor Project. There are currently four basic categories of functions that are contained in *annotate*.

- Interface functions for getting data out of specific meta-data libraries.
- Functions that support querying the different web services provided by the National Library of Medicine (NLM), and the National Center for Biotechnology Information (NCBI).
- Functions that support organizing and structuring chromosomal location data to support some of the gene plotting and gene finding routines in *geneplotter*.
- Functions that produce HTML output, hyperlinked to different web resources, from gene lists.

We will briefly describe the second and third of these different aspects and then for the remainder of this vignette concentrate on the first category. The other three have their own vignettes.

There are two different, but complementary strategies for accessing meta-data. One is to use highly curated data that have been assembled from many different sources and a second is to rely on on-line sources. The former tends to be less current but more comprehensive while the latter tends to be current but can be less comprehensive and difficult to reproduce as the sources themselves are constantly evolving. To address the second of these we develop and distribute software that can take advantage of the web services that are provided. Perhaps the richest source of these is provided by the National Library of Medicine. Further details on accessing these resources are provided in Gentleman and Gentry (2002) and Gentry (2004b).

While the chromosomal location is not always of interest, in certain situations, especially the study of genetic diseases it is important that we be able to associate particular genes with locations on chromosomes. We provide a complete set of functions that map from LocusLink identifiers to chromosomal location. Examples and further discussion are provided in Gentry (2004a).

Producing output that helps users navigate and understand the results of an analysis is a very important aspect of any data analysis. Since one of the primary tasks that is carried out when analysing gene expression data is to create lists of interesting genes we have provided some simple infrastructure that will help produce a hyperlinked output page for any given set of genes. A more substantial and comprehensive approach has been taken by C. Smith in the *annaffy* package. A vignette for using the functions provided in the *annotate* package is provided in Gentleman (2003).

We now turn our attention to interfaces to the meta-data packages and how and when they will be useful. The annotation library provides interface support for the different meta-data packages (<http://www.bioconductor.org/help/bioc-views/release/data/annotation/>) that are available through the Bioconductor Project. We have tried to make these different meta-data packages modular, in the sense that all of them should have similar sets of mappings from manufacturer IDs to specific biological data such as chromosomal location, GO, and LocusLink identifiers.

Annotation in the Bioconductor Project is handled by two systems. One, *AnnBuilder* is a system for assembling and relating the data from various sources. It is much more *industrial* and takes advantage of many different non-R tools such as Perl and XML. The second package is *annotate*. This package is designed to provide experiment level annotation resources and to help users associate the outputs of *AnnBuilder* with their particular data.

There will be some need for the structure of the meta-data packages to evolve over time and by making use of the functions provided in *annotate* users and developers should shield themselves from many of the changes. We will endeavor to keep the *annotate* interfaces constant.

Any given experiment typically involves a set of known identifiers (probes in the case of a microarray experiment). These identifiers are typically unique (for any manufacturer). This holds true for any of the standard databases such as LocusLink. However, when the identifiers from one source are linked to the identifiers from another there does not need to be a one-to-one relationship. For example, several different Affymetrix accession numbers correspond to a single LocusLink identifier. Thus, when going one direction (Affymetrix to LocusLink) we have no problem, but when going the other we need some mechanism for dealing with the multiplicity of matches.

## A Short Example

We will consider the Affymetrix human gene chip, *hgu95av2*, for our example. We first load this chip's package and *annotate*.

```
> library("annotate")
> library("hgu95av2.db")
> ls("package:hgu95av2.db")

[1] "hgu95av2"                "hgu95av2.db"            "hgu95av2ACCNUM"
[4] "hgu95av2ALIAS2PROBE"     "hgu95av2CHR"           "hgu95av2CHRLNGTHS"
[7] "hgu95av2CHRLOC"         "hgu95av2CHRLOCEND"     "hgu95av2ENSEMBL"
[10] "hgu95av2ENSEMBL2PROBE"  "hgu95av2ENTREZID"      "hgu95av2ENZYME"
```

[13]	"hgu95av2ENZYME2PROBE"	"hgu95av2GENENAME"	"hgu95av2GO"
[16]	"hgu95av2GO2ALLPROBES"	"hgu95av2GO2PROBE"	"hgu95av2MAP"
[19]	"hgu95av2MAPCOUNTS"	"hgu95av2OMIM"	"hgu95av2ORGANISM"
[22]	"hgu95av2ORGPKG"	"hgu95av2PATH"	"hgu95av2PATH2PROBE"
[25]	"hgu95av2PFAM"	"hgu95av2PMID"	"hgu95av2PMID2PROBE"
[28]	"hgu95av2PROSITE"	"hgu95av2REFSEQ"	"hgu95av2SYMBOL"
[31]	"hgu95av2UNIPROT"	"hgu95av2_dbInfo"	"hgu95av2_dbconn"
[34]	"hgu95av2_dbfile"	"hgu95av2_dbschema"	

We see the listing of twenty or thirty different R objects in this package. Most of them represent mappings from the identifiers on the Affymetrix chip to the different biological resources and you can find out more about them by using the R help system, since each has a manual page that describes the data together with other information such as where, when and what files were used to construct the mappings. Also, each meta-data package has one object that has the same name as the package basename, in this case it is `hgu95av2`. This is function and it can be invoked to find out some of the different statistics regarding the mappings that were done. Its manual page lists all data resources that were used to create the meta-data package.

```
> hgu95av2()
```

```
Quality control information for hgu95av2:
```

```
This package has the following mappings:
```

```
hgu95av2ACCNUM has 12625 mapped keys (of 12625 keys)
hgu95av2ALIAS2PROBE has 37476 mapped keys (of 261311 keys)
hgu95av2CHR has 11683 mapped keys (of 12625 keys)
hgu95av2CHRLNGTHS has 595 mapped keys (of 711 keys)
hgu95av2CHRLOC has 11637 mapped keys (of 12625 keys)
hgu95av2CHRLOCEND has 11637 mapped keys (of 12625 keys)
hgu95av2ENSEMBL has 11609 mapped keys (of 12625 keys)
hgu95av2ENSEMBL2PROBE has 10016 mapped keys (of 42248 keys)
hgu95av2ENTREZID has 11683 mapped keys (of 12625 keys)
hgu95av2ENZYME has 2137 mapped keys (of 12625 keys)
hgu95av2ENZYME2PROBE has 785 mapped keys (of 975 keys)
hgu95av2GENENAME has 11683 mapped keys (of 12625 keys)
hgu95av2GO has 11475 mapped keys (of 12625 keys)
hgu95av2GO2ALLPROBES has 20621 mapped keys (of 22286 keys)
hgu95av2GO2PROBE has 15988 mapped keys (of 18640 keys)
hgu95av2MAP has 11681 mapped keys (of 12625 keys)
hgu95av2OMIM has 11071 mapped keys (of 12625 keys)
hgu95av2PATH has 5445 mapped keys (of 12625 keys)
hgu95av2PATH2PROBE has 228 mapped keys (of 229 keys)
hgu95av2PMID has 11673 mapped keys (of 12625 keys)
hgu95av2PMID2PROBE has 570355 mapped keys (of 803747 keys)
```

hgu95av2REFSEQ has 11646 mapped keys (of 12625 keys)  
hgu95av2SYMBOL has 11683 mapped keys (of 12625 keys)  
hgu95av2UNIPROT has 11416 mapped keys (of 12625 keys)

Additional Information about this package:

DB schema: HUMANCHIP\_DB  
DB schema version: 2.1  
Organism: Homo sapiens  
Date for NCBI data: 2021-Apr14  
Date for GO data: 2021-02-01  
Date for KEGG data: 2011-Mar15  
Date for Golden Path data: 2021-Feb16  
Date for Ensembl data: 2021-Feb16

Now let's consider a specific object, say the `hgu95av2ENTREZID` object.

```
> hgu95av2ENTREZID
```

ENTREZID map for chip hgu95av2 (object of class "ProbeAnnDbBimap")

If we type its name we see that it is an R environment; all this means is that it is a special data type that is efficient at storing and retrieving mappings between symbols (the Affymetrix identifiers) and associated values (the LocusLink IDs).

We can retrieve values from this environment in many different ways (and the reader is referred to the R help pages for more details on using some of the functions described briefly here). Suppose that we are interested in finding the LocusLink ID for the Affymetrix probe, `1000_at`. Then we can do it in any one of the following ways:

```
> get("1000_at", env=hgu95av2ENTREZID)
```

```
[1] "5595"
```

```
> hgu95av2ENTREZID[["1000_at"]]
```

```
[1] "5595"
```

```
> hgu95av2ENTREZID$"1000_at"
```

```
[1] "5595"
```

```
>
```

And in all cases we see that the LocusLink identifier is 5595.

If you want to get more than one object from an environment you also have a number of choices. You can extract them one at a time using either a `for` loop or `apply` or `eapply`. It will be more efficient to use `mget` since it does the retrieval using internal code and is optimized. You may also want to turn the environment into a named list, so that you can perform different list operations on it, this can be done using the function `contents` or `as.list`.

```

> LLS = as.list(hgu95av2ENTREZID)
> length(LLs)

[1] 12625

> names(LLs)[1:10]

[1] "1000_at" "1001_at" "1002_f_at" "1003_s_at" "1004_at" "1005_at"
[7] "1006_at" "1007_s_at" "1008_f_at" "1009_at"

>

```

## 2 Developers Tips

Software developers that are building other tools that might make use of the infrastructure produced here should make use of the `get*` family of functions. Examples include `getEG`, `getGO` and so on. There are two reasons for using these functions.

First, they allow you to implement functionality that is independent of the meta-data packages. Since each of these functions takes two arguments, one a list of the manufacturers ids and the second the *basename* of the annotation package these functions will provide the correct results for all annotation packages.

A second reason to make use of these interface functions is that they are guaranteed not to change. The underlying structure of the meta-data packages may change and developers that access this directly will find that their code needs to be updated regularly. But developers that make use of these interface functions will find that their code needs much less maintenance.

## 3 Session Information

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

```

R Under development (unstable) (2025-03-01 r87860 ucrt)
Platform: x86_64-w64-mingw32/x64
Running under: Windows Server 2022 x64 (build 20348)

```

```

Matrix products: default
LAPACK version 3.12.0

```

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      datasets  
[8] methods   base
```

```
other attached packages:
```

```
[1] Rgraphviz_2.51.9      graph_1.85.3          xtable_1.8-4  
[4] GO.db_3.21.0          hgu95av2.db_3.13.0    org.Hs.eg.db_3.21.0  
[7] annotate_1.85.0       XML_3.99-0.18         AnnotationDbi_1.69.0  
[10] IRanges_2.41.3        S4Vectors_0.45.4      Biobase_2.67.0  
[13] BiocGenerics_0.53.6   generics_0.1.3        BiocStyle_2.35.0
```

```
loaded via a namespace (and not attached):
```

```
[1] bit_4.6.0              jsonlite_2.0.0         compiler_4.5.0  
[4] BiocManager_1.30.25    crayon_1.5.3           blob_1.2.4  
[7] Biostrings_2.75.4      jquerylib_0.1.4        png_0.1-8  
[10] yaml_2.3.10            fastmap_1.2.0          R6_2.6.1  
[13] XVector_0.47.2         GenomeInfoDb_1.43.4    knitr_1.50  
[16] bookdown_0.42          GenomeInfoDbData_1.2.14 DBI_1.2.3  
[19] bslib_0.9.0            rlang_1.1.5            KEGGREST_1.47.0  
[22] cachem_1.1.0           xfun_0.51              sass_0.4.9  
[25] bit64_4.6.0-1          RSQLite_2.3.9          memoise_2.0.1  
[28] cli_3.6.4              digest_0.6.37          lifecycle_1.0.4  
[31] vctrs_0.6.5            evaluate_1.0.3         rmarkdown_2.29  
[34] httr_1.4.7             pkgconfig_2.0.3        tools_4.5.0  
[37] htmltools_0.5.8.1      UCSC.utils_1.3.1
```

## References

- R. Gentleman. Howto: get pretty html output for my gene list. *Bioconductor Vignettes*, 2003. URL <http://www.bioconductor.org>.
- R. Gentleman and J. Gentry. Querying pubmed. *R News*, 2(2):28–31, June 2002. URL <http://CRAN.R-project.org/doc/Rnews/>.
- J. Gentry. Howto: Build and use chromosomal information. *Bioconductor Vignettes*, 2004a. URL <http://www.bioconductor.org>.
- J. Gentry. Howto: Automated querying of pubmed data. *Bioconductor Vignettes*, 2004b. URL <http://www.bioconductor.org>.