

How to use bimap from the ".db" annotation packages

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NOTE The 'bimap' interface to annotation resources is not recommended; instead, use the approach in the vignette [Introduction To Bioconductor Annotation Packages](#).

1 Introduction

1.0.1 Purpose

AnnotationDbi is used primarily to create mapping objects that allow easy access from R to underlying annotation databases. As such, it acts as the R interface for all the standard annotation packages. Underlying each AnnotationDbi supported annotation package is at least one (and often two) annotation databases. AnnotationDbi also provides schemas for these databases. For each supported model organism, a standard gene centric database is maintained from public sources and is packaged up as an appropriate organism or "org" package.

1.0.2 Database Schemas

For developers, a lot of the benefits of having the information loaded into a real database will require some knowledge about the database schema. For this reason the schemas that were used in the creation of each database type are included in AnnotationDbi. The currently supported schemas are listed in the DBSchemas directory of AnnotationDbi. But it is also possible to simply print out the schema that a package is currently using by using its "_dbschema" method.

There is one schema/database in each kind of package. These schemas specify which tables and indices will be present for each package of that type. The schema that a particular package is using is also listed when you type the name of the package as a function to obtain quality control information.

The code to make most kinds of the new database packages is also included in AnnotationDbi. Please see the vignette on SQLForge for more details on how to make additional database packages.

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1.0.3 Internal schema Design of org packages

The current design of the organism packages is deliberately simple and gene centric. Each table in the database contains a unique kind of information and also an internal identifier called `_id`. The internal `_id` has no meaning outside of the context of a single database. But `_id` does connect all the data within a single database.

As an example if we wanted to connect the values in the genes table with the values in the kegg table, we could simply join the two tables using the internal `_id` column. It is very important to note however that `_id` does not have any absolute significance. That is, it has no meaning outside of the context of the database where it is used. It is tempting to think that an `_id` could have such significance because within a single database, it looks and behaves similarly to an entrez gene ID. But `_id` is definitely NOT an entrez gene ID. The entrez gene IDs are in another table entirely, and can be connected to using the internal `_id` just like all the other meaningful information inside these databases. Each organism package is centered around one type of gene identifier. This identifier is found as the `gene_id` field in the genes table and is both the central ID for the database as well as the foreign key that chip packages should join to.

The chip packages are 'lightweight', and only contain information about the basic probe to gene mapping. You might wonder how such packages can provide access to all the other information that they do. This is possible because all the other data provided by chip packages comes from joins that are performed by AnnotationDbi behind the scenes at run time. All chip packages have a dependency on at least one organism package. The name of the organism package being depended on can be found by looking at its "ORGPKG" value. To learn about the schema from the appropriate organism package, you will need to look at the "`_dbschema`" method for that package. In the case of the chip packages, the `gene_id` that in these packages is mapped to the `probe_ids`, is used as a foreign key to the appropriate organism package.

Specialized packages like the packages for GO and KEGG, will have their own schemas but will also adhere to the use of an internal `_id` for joins between their tables. As with the organism packages, this `_id` is not suitable for use as a foreign key.

For a complete listing of the different schemas used by various packages, users can use the `available.dbschemas` function. This list will also tell you which model organisms are supported.

```
library(DBI)
library(org.Hs.eg.db)

## Loading required package: AnnotationDbi
## Loading required package: stats4
## Loading required package: BiocGenerics
## Loading required package: parallel
```

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```
##
## Attaching package: 'BiocGenerics'

## The following objects are masked from 'package:parallel':
##
##   clusterApply, clusterApplyLB, clusterCall, clusterEvalQ,
##   clusterExport, clusterMap, parApply, parCapply, parLapply,
##   parLapplyLB, parRapply, parSapply, parSapplyLB

## The following objects are masked from 'package:stats':
##
##   IQR, mad, sd, var, xtabs

## The following objects are masked from 'package:base':
##
##   Filter, Find, Map, Position, Reduce, anyDuplicated, append,
##   as.data.frame, cbind, colMeans, colSums, colnames, do.call,
##   duplicated, eval, evalq, get, grep, grepl, intersect,
##   is.unsorted, lapply, lengths, mapply, match, mget, order, paste,
##   pmax, pmax.int, pmin, pmin.int, rank, rbind, rowMeans, rowSums,
##   rownames, sapply, setdiff, sort, table, tapply, union, unique,
##   unsplit, which, which.max, which.min

## Loading required package: Biobase

## Welcome to Bioconductor
##
##   Vignettes contain introductory material; view with
##   'browseVignettes()'. To cite Bioconductor, see
##   'citation("Biobase")', and for packages 'citation("pkgname)".

## Loading required package: IRanges

## Loading required package: S4Vectors

##
## Attaching package: 'S4Vectors'

## The following object is masked from 'package:base':
##
##   expand.grid

##
library(AnnotationForge)
available.dbschemas()
```

2 Examples

2.0.1 Basic information

The *AnnotationDbi* package provides an interface to SQLite-based annotation packages. Each SQLite-based annotation package (identified by a ".db" suffix in the package name) contains a number of *AnnDbBimap* objects in place of the *environment* objects found in the old-style environment-based annotation packages. The API provided by *AnnotationDbi* allows you to treat the *AnnDbBimap* objects like *environment* instances. For example, the functions `[`, `get`, `mget`, and `ls` all behave the same as they did with the older environment based annotation packages. In addition, new methods like `[`, `toTable`, `subset` and others provide some additional flexibility in accessing the annotation data.

```
library(hgu95av2.db)

##
```

The same basic set of objects is provided with the db packages:

```
ls("package:hgu95av2.db")

## [1] "hgu95av2"                "hgu95av2.db"
## [3] "hgu95av2ACCNUM"          "hgu95av2ALIAS2PROBE"
## [5] "hgu95av2CHR"             "hgu95av2CHRLNGTHS"
## [7] "hgu95av2CHRLLOC"         "hgu95av2CHRLLOCEND"
## [9] "hgu95av2ENSEMBL"         "hgu95av2ENSEMBL2PROBE"
## [11] "hgu95av2ENTREZID"        "hgu95av2ENZYME"
## [13] "hgu95av2ENZYME2PROBE"    "hgu95av2GENENAME"
## [15] "hgu95av2G0"              "hgu95av2G02ALLPROBES"
## [17] "hgu95av2G02PROBE"        "hgu95av2MAP"
## [19] "hgu95av2MAPCOUNTS"      "hgu95av2OMIM"
## [21] "hgu95av2ORGANISM"        "hgu95av2ORGPKG"
## [23] "hgu95av2PATH"            "hgu95av2PATH2PROBE"
## [25] "hgu95av2PFAM"            "hgu95av2PMID"
## [27] "hgu95av2PMID2PROBE"      "hgu95av2PROSITE"
## [29] "hgu95av2REFSEQ"          "hgu95av2SYMBOL"
## [31] "hgu95av2UNIGENE"         "hgu95av2UNIPROT"
## [33] "hgu95av2_dbInfo"         "hgu95av2_dbconn"
## [35] "hgu95av2_dbfile"         "hgu95av2_dbschema"
```

Exercise 1

Start an R session and use the `library` function to load the `hgu95av2.db` software package. Use `search()` to see that an organism package was also loaded and then use the appropriate `"_dbschema"` methods to the schema for the `hgu95av2.db` and `org.Hs.eg.db` packages.

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It is possible to call the package name as a function to get some QC information about it.

```
qcdata = capture.output(hgu95av2())
head(qcdata, 20)

## [1] "Quality control information for hgu95av2:"
## [2] ""
## [3] ""
## [4] "This package has the following mappings:"
## [5] ""
## [6] "hgu95av2ACCNUM has 12625 mapped keys (of 12625 keys)"
## [7] "hgu95av2ALIAS2PROBE has 34238 mapped keys (of 120180 keys)"
## [8] "hgu95av2CHR has 11472 mapped keys (of 12625 keys)"
## [9] "hgu95av2CHRLNGTHS has 93 mapped keys (of 455 keys)"
## [10] "hgu95av2CHRLC has 11423 mapped keys (of 12625 keys)"
## [11] "hgu95av2CHRLCEND has 11423 mapped keys (of 12625 keys)"
## [12] "hgu95av2ENSEMBL has 11365 mapped keys (of 12625 keys)"
## [13] "hgu95av2ENSEMBL2PROBE has 9545 mapped keys (of 28931 keys)"
## [14] "hgu95av2ENTREZID has 11474 mapped keys (of 12625 keys)"
## [15] "hgu95av2ENZYME has 2097 mapped keys (of 12625 keys)"
## [16] "hgu95av2ENZYME2PROBE has 779 mapped keys (of 975 keys)"
## [17] "hgu95av2GENENAME has 11474 mapped keys (of 12625 keys)"
## [18] "hgu95av2G0 has 11229 mapped keys (of 12625 keys)"
## [19] "hgu95av2G02ALLPROBES has 18521 mapped keys (of 21861 keys)"
## [20] "hgu95av2G02PROBE has 13971 mapped keys (of 17120 keys)"
```

Alternatively, you can get similar information on how many items are in each of the provided maps by looking at the MAPCOUNTs:

```
hgu95av2MAPCOUNTS
```

To demonstrate the *environment* API, we'll start with a random sample of probe set IDs.

```
all_probes <- ls(hgu95av2ENTREZID)
length(all_probes)

## [1] 12625

set.seed(0xa1beef)
probes <- sample(all_probes, 5)
probes

## [1] "31882_at" "38780_at" "37033_s_at" "1702_at" "31610_at"
```

The usual ways of accessing annotation data are also available.

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```
hgu95av2ENTREZID[[probes[1]]]
## [1] "9136"
hgu95av2ENTREZID$"31882_at"
## [1] "9136"
syms <- unlist(mget(probes, hgu95av2SYMBOL))
syms
##      31882_at      38780_at 37033_s_at      1702_at      31610_at
##      "RRP9"      "AKR1A1"      "GPX1"      "IL2RA" "PDZK1IP1"
```

The annotation packages provide a huge variety of information in each package. Some common types of information include gene symbols (SYMBOL), GO terms (GO), KEGG pathway IDs (KEGG), ENSEMBL IDs (ENSEMBL) and chromosome start and stop locations (CHRLOC and CHRLOCEND). Each mapping will have a manual page that you can read to describe the data in the mapping and where it came from.

```
?hgu95av2CHRLOC
```

Exercise 2

For the probes in 'probes' above, use the annotation mappings to find the chromosome start locations.

2.0.2 Manipulating Bimap Objects

Many filtering operations on the annotation *Bimap* objects require conversion of the *AnnDbBimap* into a *list*. In general, converting to lists will not be the most efficient way to filter the annotation data when using a SQLite-based package. Compare the following two examples for how you could get the 1st ten elements of the hgu95av2SYMBOL mapping. In the 1st case we have to get the entire mapping into list form, but in the second case we first subset the mapping object itself and this allows us to only convert the ten elements that we care about.

```
system.time(as.list(hgu95av2SYMBOL)[1:10])

## vs:

system.time(as.list(hgu95av2SYMBOL[1:10]))
```

There are many different kinds of *Bimap* objects in AnnotationDbi, but most of them are of class *AnnDbBimap*. All *RclassBimap* objects represent data as a set of left and right keys. The typical usage of these mappings is to search for right keys that match a set of left keys that have been supplied by the user. But sometimes it is also convenient to go in the opposite direction.

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The annotation packages provide many reverse maps as objects in the package name space for backwards compatibility, but the reverse mappings of almost any map is also available using `revmap`. Since the data are stored as tables, no extra disk space is needed to provide reverse mappings.

```
unlist(mget(syms, revmap(hgu95av2SYMBOL)))  
##          RRP9          AKR1A1          GPX1          IL2RA          PDZK1IP1  
## "31882_at" "38780_at" "37033_s_at" "1702_at" "31610_at"
```

So now that you know about the `revmap` function you might try something like this:

```
as.list(revmap(hgu95av2PATH) ["00300"])  
## $`00300`  
## [1] "36132_at" "35870_at"
```

Note that in the case of the PATH map, we don't need to use `revmap(x)` because `hgu95av2.db` already provides the PATH2PROBE map:

```
x <- hgu95av2PATH  
## except for the name, this is exactly revmap(x)  
revx <- hgu95av2PATH2PROBE  
revx2 <- revmap(x, objName="PATH2PROBE")  
revx2  
  
## PATH2PROBE map for chip hgu95av2 (object of class "ProbeAnnDbBimap")  
identical(revx, revx2)  
## [1] TRUE  
as.list(revx["00300"])  
## $`00300`  
## [1] "36132_at" "35870_at"
```

Note that most maps are reversible with `revmap`, but some (such as the more complex GO mappings), are not. Why is this? Because to reverse a mapping means that there has to be a "value" that will always become the "key" on the newly reversed map. And GO mappings have several distinct possibilities to choose from (GO ID, Evidence code or Ontology). In non-reversible cases like this, AnnotationDbi will usually provide a pre-defined reverse map. That way, you will always know what you are getting when you call `revmap`.

While we are on the subject of GO and GO mappings, there are a series of special methods for GO mappings that can be called to find out details about these IDs. `Term`, `GOID`, `Ontology`, `Definition`, `Synonym`, and `Secondary` are all useful ways of getting additional information about a particular GO ID. For example:

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```
Term("GO:0000018")

## Loading required package: GO.db

##

##              GO:0000018
## "regulation of DNA recombination"

Definition("GO:0000018")

##

## "Any process that modulates the frequency, rate or extent of DNA recombination, a DNA metabolic
```

Exercise 3

Given the following set of RefSeq IDs: `c("NG_005114", "NG_007432", "NG_008063")`, Find the Entrez Gene IDs that would correspond to those. Then find the GO terms that are associated with those entrez gene IDs.

`org.Hs.eg.db` packages.

2.0.3 The Contents and Structure of Bimap Objects

Sometimes you may want to display or subset elements from an individual map. A *Bimap* interface is available to access the data in table (*data.frame*) format using `[` and `toTable`.

```
head(toTable(hgu95av2G0[probes]))

##  probe_id      go_id Evidence Ontology
## 1  1702_at GO:0000165      TAS      BP
## 2  1702_at GO:0002437      IEA      BP
## 3  1702_at GO:0002664      IMP      BP
## 4  1702_at GO:0006915      TAS      BP
## 5  1702_at GO:0006924      IEA      BP
## 6  1702_at GO:0006954      IBA      BP
```

The `toTable` function will display all of the information in a *Bimap*. This includes both the left and right values along with any other attributes that might be attached to those values. The left and right keys of the *Bimap* can be extracted using `Lkeys` and `Rkeys`. If it is necessary to only display information that is directly associated with the left to right links in a *Bimap*, then the `links` function can be used. The `links` returns a data frame with one row for each link in the *bimap* that it is applied to. It only reports the left and right keys along with any attributes that are attached to the edge between these two values.

Note that the order of the cols returned by `toTable` does not depend on the direction of the map. We refer to it as an 'undirected method':

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```
toTable(x)[1:6, ]  
  
##   probe_id path_id  
## 1 1000_at  04010  
## 2 1000_at  04012  
## 3 1000_at  04062  
## 4 1000_at  04114  
## 5 1000_at  04150  
## 6 1000_at  04270  
  
toTable(revx)[1:6, ]  
  
##   probe_id path_id  
## 1 1000_at  04010  
## 2 1000_at  04012  
## 3 1000_at  04062  
## 4 1000_at  04114  
## 5 1000_at  04150  
## 6 1000_at  04270
```

Notice however that the Lkeys are always on the left (1st col), the Rkeys always in the 2nd col

For `length()` and `keys()`, the result does depend on the direction, hence we refer to these as 'directed methods':

```
length(x)  
## [1] 12625  
  
length(revx)  
## [1] 229  
  
allProbeSetIds <- keys(x)  
allKEGGIds <- keys(revx)
```

There are more 'undirected' methods listed below:

```
junk <- Lkeys(x)           # same for all maps in hgu95av2.db (except pseudo-map  
                           # MAPCOUNTS)  
Llength(x)                # nb of Lkeys  
## [1] 12625  
  
junk <- Rkeys(x)           # KEGG ids for PATH/PATH2PROBE maps, GO ids for  
                           # GO/GO2PROBE/GO2ALLPROBES maps, etc...  
Rlength(x)                # nb of Rkeys  
## [1] 229
```

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Notice how they give the same result for `x` and `revmap(x)`

You might be tempted to think that `Lkeys` and `Llength` will tell you all that you want to know about the left keys. But things are more complex than this, because not all keys are mapped. Often, you will only want to know about the keys that are mapped (ie. the ones that have a corresponding Rkey). To learn this you want to use the `mappedkeys` or the undirected variants `mappedLkeys` and `mappedRkeys`. Similarly, the `count.mappedkeys`, `count.mappedLkeys` and `count.mappedRkeys` methods are very fast ways to determine how many keys are mapped. Accessing keys like this is usually very fast and so it can be a decent strategy to subset the mapping by 1st using the mapped keys that you want to find.

```
x = hgu95av2ENTREZID[1:10]
## Directed methods
mappedkeys(x)          # mapped keys

## [1] "1000_at"  "1001_at"  "1002_f_at" "1003_s_at" "1004_at"
## [6] "1005_at"  "1006_at"  "1008_f_at" "1009_at"

count.mappedkeys(x)    # nb of mapped keys

## [1] 9

## Undirected methods
mappedLkeys(x)         # mapped left keys

## [1] "1000_at"  "1001_at"  "1002_f_at" "1003_s_at" "1004_at"
## [6] "1005_at"  "1006_at"  "1008_f_at" "1009_at"

count.mappedLkeys(x)   # nb of mapped Lkeys

## [1] 9
```

If you want to find keys that are not mapped to anything, you might want to use `isNA`.

```
y = hgu95av2ENTREZID[isNA(hgu95av2ENTREZID)] # usage like is.na()
Lkeys(y)[1:4]

## [1] "1007_s_at" "1047_s_at" "1089_i_at" "108_g_at"
```

Exercise 4

How many probesets do not have a GO mapping for the `hgu95av2.db` package? How many have no mapping? Find a probeset that has a GO mapping. Now look at the GO mappings for this probeset in table form.

2.0.4 Some specific examples

Lets use what we have learned to get information about the probes that are not assigned to a chromosome:

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```
x <- hgu95av2CHR
Rkeys(x)

## [1] "19" "12" "8" "14" "3" "2" "17" "16" "9" "X" "6" "1" "7"
## [14] "10" "11" "22" "5" "18" "15" "Y" "20" "21" "4" "13" "MT" "Un"

chroms <- Rkeys(x)[23:24]
chroms

## [1] "4" "13"

Rkeys(x) <- chroms
toTable(x)

##      probe_id chromosome
## 1    1029_s_at         4
## 2    1036_at         4
## 3    1058_at        13
## 4    1065_at        13
## 5    1115_at         4
## 6    1189_at        13
## 7    1198_at        13
## 8    1219_at         4
## 9    1220_g_at         4
## 10   1249_at         4
## 11   1285_at         4
## 12   1303_at         4
## 13   1325_at         4
## 14   1348_s_at        13
## 15   1369_s_at         4
## 16   1377_at         4
## 17   1378_g_at         4
## 18   1451_s_at        13
## 19   1503_at        13
## 20   1507_s_at         4
## 21   1527_s_at        13
## 22   1528_at        13
## 23   1529_at        13
## 24   1530_g_at        13
## 25   1531_at        13
## 26   1532_g_at        13
## 27   1538_s_at         4
## 28   1542_at         4
## 29   1545_g_at        13
## 30   1567_at        13
## 31   1570_f_at        13
## 32   1571_f_at        13
```

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```
## 33      1593_at      4
## 34      1597_at     13
## 35     1598_g_at     13
## 36       159_at      4
## 37     1600_at      4
## 38     1604_at      4
## 39     1605_g_at      4
## 40     1616_at     13
## 41     1624_at      4
## 42     1629_s_at      4
## 43     1670_at     13
## 44     1672_f_at     13
## 45     1679_at      4
## 46     1708_at      4
## 47     1709_g_at      4
## 48       170_at     13
## 49     1720_at      4
## 50     1721_g_at      4
## 51     1731_at      4
## 52     1732_at      4
## 53     1819_at     13
## 54     1828_s_at      4
## 55     1836_at      4
## 56     1883_s_at      4
## 57     1888_s_at      4
## 58     1900_at     13
## 59     1905_s_at     13
## 60     1913_at      4
## 61     1914_at     13
## 62     1931_at     13
## 63     1934_s_at      4
## 64     1943_at      4
## 65     1954_at      4
## 66     1963_at     13
## 67     1964_g_at     13
## 68     1987_at      4
## 69     1988_at      4
## 70     1989_at     13
## 71     1990_g_at     13
## 72     2044_s_at     13
## 73     2062_at      4
## 74     2092_s_at      4
## 75       214_at      4
## 76     215_g_at      4
## 77     252_at     13
```

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```
## 78 253_g_at      13
## 79 260_at        4
## 80 281_s_at      4
## 81 31314_at      4
## 82 31320_at      13
## 83 31333_at      4
## 84 31345_at      4
## 85 31349_at      4
## 86 31356_at      4
## 87 31382_f_at    4
## 88 31404_at      13
## 89 31408_at      4
## 90 31464_at      13
## 91 31465_g_at    13
## 92 31516_f_at    13
## 93 31543_at      4
## 94 31562_at      13
## 95 31584_at      13
## 96 31628_at      13
## 97 31631_f_at    4
## 98 31639_f_at    13
## 99 31640_r_at    13
## 100 31670_s_at    4
## 101 31684_at      4
## 102 31706_at      4
## 103 31744_at      4
## 104 31753_at     13
## 105 31790_at     13
## 106 31792_at      4
## 107 31805_at      4
## 108 31811_r_at    4
## 109 31847_at     13
## 110 31849_at     13
## 111 31851_at     13
## 112 31876_r_at    4
## 113 31894_at      4
## 114 31969_i_at    4
## 115 31970_r_at    4
## 116 32006_r_at    4
## 117 32026_s_at    4
## 118 32080_at      4
## 119 32102_at     13
## 120 32145_at      4
## 121 32146_s_at    4
## 122 32147_at     13
```

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```
## 123 32148_at      13
## 124 32163_f_at    4
## 125 32180_s_at    4
## 126 32220_at      13
## 127 32299_at      4
## 128 32349_at      4
## 129 32353_at      4
## 130 32357_at      4
## 131 32368_at      13
## 132 32393_s_at    4
## 133 32439_at      13
## 134 32446_at      4
## 135 32449_at      4
## 136 32465_at      4
## 137 32482_at      13
## 138 32506_at      4
## 139 32507_at      4
## 140 32570_at      4
## 141 32580_at      4
## 142 32595_at      4
## 143 32602_at      4
## 144 32641_at      13
## 145 32675_at      4
## 146 32703_at      4
## 147 32768_at      13
## 148 32769_at      4
## 149 32770_at      4
## 150 32771_at      4
## 151 32812_at      4
## 152 32822_at      4
## 153 32832_at      4
## 154 32862_at      13
## 155 32906_at      13
## 156 32979_at      4
## 157 32986_s_at    13
## 158 32998_at      4
## 159 33013_at      4
## 160 33068_f_at    4
## 161 33069_f_at    4
## 162 33100_at      4
## 163 33150_at      4
## 164 33151_s_at    4
## 165 33155_at      4
## 166 33156_at      4
## 167 33168_at      13
```

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```
## 168 33171_s_at      4
## 169  33172_at      4
## 170 33173_g_at      4
## 171  33199_at     13
## 172  33208_at     13
## 173  33241_at      4
## 174  33249_at      4
## 175  33267_at      4
## 176  33276_at     13
## 177  33299_at      4
## 178  33318_at     13
## 179  33356_at      4
## 180  33359_at      4
## 181  33369_at      4
## 182 33370_r_at      4
## 183  33382_at      4
## 184  33483_at      4
## 185  33488_at      4
## 186  33490_at      4
## 187  33494_at      4
## 188  33519_at      4
## 189  33520_at     13
## 190  33525_at      4
## 191  33526_at      4
## 192  33529_at      4
## 193  33536_at      4
## 194  33544_at      4
## 195  33564_at      4
## 196  33576_at     13
## 197  33584_at      4
## 198  33596_at      4
## 199  33657_at      4
## 200 33672_f_at      4
## 201 33673_r_at      4
## 202  33687_at     13
## 203  33700_at     13
## 204  33733_at      4
## 205  33791_at     13
## 206  33823_at      4
## 207  33827_at     13
## 208  33837_at      4
## 209  33859_at     13
## 210  33975_at      4
## 211  33990_at      4
## 212 33991_g_at      4
```

How to use bimap from the ".db" annotation packages

```
## 213 33992_at      4
## 214 33997_at      4
## 215 34021_at      4
## 216 34022_at      4
## 217 34026_at     13
## 218 34029_at      4
## 219 34048_at      4
## 220 34051_at     13
## 221 34058_at      4
## 222 34075_at      4
## 223 34122_at      4
## 224 34131_at      4
## 225 34144_at      4
## 226 34145_at      4
## 227 34149_at      4
## 228 34170_s_at    4
## 229 34181_at      4
## 230 34198_at      4
## 231 34211_at     13
## 232 34239_at     13
## 233 34240_s_at    13
## 234 34247_at      4
## 235 34248_at      4
## 236 34275_s_at    4
## 237 34284_at     13
## 238 34307_at     13
## 239 34319_at      4
## 240 34324_at     13
## 241 34334_at     13
## 242 34335_at     13
## 243 34341_at      4
## 244 34342_s_at    4
## 245 34353_at      4
## 246 34398_at     13
## 247 34411_at      4
## 248 34423_at      4
## 249 34459_at     13
## 250 34476_r_at    4
## 251 34482_at      4
## 252 34512_at      4
## 253 34551_at      4
## 254 34564_at      4
## 255 34565_at      4
## 256 34578_at     13
## 257 34583_at     13
```


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```
## 258 34596_at      4
## 259 34637_f_at    4
## 260 34638_r_at    4
## 261 34657_at     13
## 262 34672_at     13
## 263 34745_at      4
## 264 34803_at     13
## 265 34898_at      4
## 266 34953_i_at    4
## 267 34954_r_at    4
## 268 34955_at     13
## 269 34973_at      4
## 270 34984_at      4
## 271 34988_at      4
## 272 35020_at      4
## 273 35021_at      4
## 274 35025_at      4
## 275 35028_at      4
## 276 35039_at      4
## 277 35053_at      4
## 278 35061_at      4
## 279 35063_at      4
## 280 35081_at     13
## 281 35105_at     13
## 282 35107_at     13
## 283 35110_at     13
## 284 35131_at      4
## 285 35134_at      4
## 286 35140_at     13
## 287 35147_at     13
## 288 35164_at      4
## 289 35181_at      4
## 290 35182_f_at    4
## 291 35193_at     13
## 292 35213_at     13
## 293 35214_at      4
## 294 35215_at      4
## 295 35220_at      4
## 296 35285_at      4
## 297 35306_at      4
## 298 35344_at     13
## 299 35356_at      4
## 300 35357_at      4
## 301 35371_at      4
## 302 35372_r_at    4
```

How to use bimap from the ".db" annotation packages

```
## 303 35400_at      13
## 304 35410_at       4
## 305 35435_s_at     4
## 306 35437_at       4
## 307 35469_at      13
## 308 35470_at      13
## 309 35471_g_at     13
## 310 35481_at      13
## 311 35507_at       4
## 312 35523_at       4
## 313 35554_f_at     13
## 314 35555_r_at     13
## 315 35564_at       4
## 316 35591_at       4
## 317 35656_at      13
## 318 35662_at       4
## 319 35664_at       4
## 320 35678_at       4
## 321 35698_at       4
## 322 35725_at      13
## 323 35730_at       4
## 324 35777_at       4
## 325 35793_at       4
## 326 35827_at       4
## 327 35837_at       4
## 328 35845_at       4
## 329 35871_s_at     4
## 330 35877_at      13
## 331 35904_at      13
## 332 35939_s_at     13
## 333 35940_at      13
## 334 35949_at      13
## 335 35972_at      13
## 336 35989_at       4
## 337 35991_at       4
## 338 36012_at      13
## 339 36013_at       4
## 340 36017_at      13
## 341 36021_at       4
## 342 36031_at      13
## 343 36046_at       4
## 344 36047_at       4
## 345 36065_at       4
## 346 36080_at       4
## 347 36143_at       4
```

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```
## 348 36157_at      4
## 349 36188_at     13
## 350 36194_at      4
## 351 36212_at     13
## 352 36243_at      4
## 353 36247_f_at    4
## 354 36269_at      4
## 355 36274_at     13
## 356 36358_at      4
## 357 36363_at      4
## 358 36433_at      4
## 359 36434_r_at    4
## 360 36510_at     13
## 361 36521_at     13
## 362 36606_at      4
## 363 36622_at      4
## 364 36627_at      4
## 365 36659_at     13
## 366 36717_at      4
## 367 36788_at     13
## 368 367_at       13
## 369 36814_at      4
## 370 36830_at     13
## 371 36913_at      4
## 372 36914_at      4
## 373 36915_at      4
## 374 36918_at      4
## 375 36939_at      4
## 376 36968_s_at   13
## 377 36990_at      4
## 378 37006_at      4
## 379 37019_at      4
## 380 37023_at     13
## 381 37056_at      4
## 382 37058_at      4
## 383 37062_at      4
## 384 37067_at     13
## 385 37079_at     13
## 386 37099_at     13
## 387 37109_at     13
## 388 37154_at     13
## 389 37170_at      4
## 390 37172_at     13
## 391 37173_at      4
## 392 37187_at      4
```

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```
## 393 37206_at      4
## 394 37219_at      4
## 395 37223_at      4
## 396 37243_at      4
## 397 37244_at     13
## 398 37280_at      4
## 399 37282_at      4
## 400 37291_r_at     4
## 401 37303_at     13
## 402 37322_s_at      4
## 403 37323_r_at      4
## 404 37356_r_at      4
## 405 37366_at      4
## 406 37404_at      4
## 407 37416_at      4
## 408 37472_at      4
## 409 37518_at     13
## 410 37520_at      4
## 411 37521_s_at      4
## 412 37522_r_at      4
## 413 37571_at     13
## 414 37578_at      4
## 415 37593_at     13
## 416 37619_at      4
## 417 37658_at     13
## 418 37707_i_at      4
## 419 37708_r_at      4
## 420 37723_at      4
## 421 37747_at      4
## 422 37748_at      4
## 423 37752_at      4
## 424 37757_at     13
## 425 37767_at      4
## 426 37840_at      4
## 427 37852_at      4
## 428 37926_at     13
## 429 37930_at     13
## 430 37964_at      4
## 431 38008_at      4
## 432 38016_at      4
## 433 38024_at      4
## 434 38025_r_at      4
## 435 38035_at     13
## 436 38065_at      4
## 437 38102_at     13
```

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```
## 438 38120_at      4
## 439 38168_at      4
## 440 38254_at      4
## 441 38304_r_at    13
## 442 38353_at      13
## 443 38375_at      13
## 444 38438_at      4
## 445 38485_at      4
## 446 38488_s_at    4
## 447 38489_at      4
## 448 38587_at      4
## 449 38606_at      4
## 450 38615_at      13
## 451 38643_at      4
## 452 38649_at      13
## 453 38714_at      4
## 454 38715_at      4
## 455 38736_at      4
## 456 38751_i_at    4
## 457 38752_r_at    4
## 458 38767_at      4
## 459 38768_at      4
## 460 38778_at      4
## 461 38821_at      4
## 462 38825_at      4
## 463 38838_at      4
## 464 38854_at      4
## 465 38891_at      4
## 466 38957_at      13
## 467 38972_at      13
## 468 38988_at      4
## 469 39028_at      13
## 470 39032_at      13
## 471 39037_at      4
## 472 39056_at      4
## 473 39083_at      4
## 474 39131_at      13
## 475 39132_at      4
## 476 39208_i_at    4
## 477 39209_r_at    4
## 478 39256_at      13
## 479 39257_at      13
## 480 39269_at      13
## 481 39295_s_at    4
## 482 39333_at      13
```

How to use bimap from the ".db" annotation packages

```
## 483 39337_at      4
## 484 39355_at      4
## 485 39369_at      4
## 486 39380_at      4
## 487 39382_at      4
## 488 39469_s_at    13
## 489 39475_at      4
## 490 39481_at      4
## 491 39488_at      13
## 492 39489_g_at    13
## 493 39535_at      4
## 494 39536_at      4
## 495 39554_at      4
## 496 39555_at      4
## 497 39576_at      4
## 498 39579_at      13
## 499 39600_at      4
## 500 39634_at      4
## 501 39662_s_at    4
## 502 39665_at      4
## 503 39680_at      4
## 504 39690_at      4
## 505 39698_at      4
## 506 39734_at      4
## 507 39746_at      4
## 508 39748_at      13
## 509 39758_f_at    13
## 510 39777_at      13
## 511 39786_at      4
## 512 39847_at      4
## 513 39850_at      4
## 514 39851_at      4
## 515 39852_at      13
## 516 39878_at      13
## 517 39897_at      4
## 518 39924_at      13
## 519 39929_at      4
## 520 39960_at      4
## 521 39979_at      13
## 522 40018_at      13
## 523 40058_s_at    4
## 524 40059_r_at    4
## 525 40060_r_at    4
## 526 40067_at      13
## 527 40072_at      13
```

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```
## 528 40082_at      4
## 529   400_at     13
## 530 40114_at      4
## 531 40121_at      4
## 532 40148_at      4
## 533 40180_at     13
## 534 40181_f_at   13
## 535 40199_at      4
## 536 40217_s_at    4
## 537 40218_at      4
## 538 40225_at      4
## 539 40226_at      4
## 540 40272_at      4
## 541 40310_at      4
## 542 40312_at     13
## 543 40323_at      4
## 544 40349_at      4
## 545 40354_at      4
## 546 40392_at     13
## 547 40404_s_at   13
## 548 40449_at      4
## 549 40454_at      4
## 550 40456_at      4
## 551 40473_at     13
## 552 40492_at      4
## 553 40530_at      4
## 554 40570_at     13
## 555 40576_f_at    4
## 556 40633_at     13
## 557 40681_at     13
## 558 40697_at      4
## 559 40710_at      4
## 560 40711_at      4
## 561 40727_at      4
## 562 40746_at      4
## 563 40770_f_at    4
## 564 40772_at      4
## 565 40773_at      4
## 566 40818_at      4
## 567 40828_at     13
## 568 40839_at     13
## 569 40853_at      4
## 570 40880_r_at    4
## 571 40893_at     13
## 572   408_at      4
```

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```
## 573 40908_r_at      13
## 574  40943_at       4
## 575  40970_at      13
## 576  40989_at       4
## 577  40990_at       4
## 578  40991_at       4
## 579 40992_s_at      4
## 580 40993_r_at      4
## 581 41014_s_at      4
## 582 41024_f_at      4
## 583 41025_r_at      4
## 584 41026_f_at      4
## 585  41069_at      13
## 586  41071_at       4
## 587  41104_at       4
## 588  41118_at      13
## 589 41119_f_at      13
## 590  41145_at       4
## 591  41148_at       4
## 592  41182_at      13
## 593  41191_at       4
## 594  41276_at      13
## 595  41277_at      13
## 596 41300_s_at      13
## 597  41301_at      13
## 598  41308_at       4
## 599 41309_g_at      4
## 600  41317_at      13
## 601 41318_g_at      13
## 602  41319_at      13
## 603 41376_i_at      4
## 604 41377_f_at      4
## 605  41391_at       4
## 606  41392_at       4
## 607  41402_at       4
## 608  41434_at       4
## 609  41436_at      13
## 610  41456_at       4
## 611  41459_at      13
## 612  41470_at       4
## 613 41491_s_at      13
## 614 41492_r_at      13
## 615  41493_at      13
## 616  41534_at       4
## 617  41555_at       4
```


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```
## 618 41556_s_at      4
## 619  41585_at      4
## 620 41667_s_at     13
## 621 41668_r_at     13
## 622  41697_at      4
## 623  41801_at      4
## 624  41806_at      4
## 625  41860_at     13
## 626   431_at       4
## 627   504_at       4
## 628  507_s_at      4
## 629   579_at       4
## 630   618_at       4
## 631   630_at       4
## 632  631_g_at      4
## 633   655_at       4
## 634  690_s_at       4
## 635  692_s_at       4
## 636  764_s_at       4
## 637   820_at       4
## 638   886_at       4
## 639   931_at     13
## 640  936_s_at       4
## 641  948_s_at       4
## 642   963_at     13
## 643   975_at       4
## 644   990_at     13
## 645  991_g_at     13
```

To get this in the classic named-list format:

```
z <- as.list(revmap(x)[chroms])
names(z)

## [1] "4"  "13"

z[["Y"]]

## NULL
```

Many of the common methods for accessing *Bimap* objects return things in list format. This can be convenient. But you have to be careful about this if you want to use `unlist()`. For example the following will return multiple probes for each chromosome:

```
chrs = c("12", "6")
mget(chrs, revmap(hgu95av2CHR[1:30]), ifnotfound=NA)
```

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```
## $`12`  
## [1] "1018_at" "1019_g_at" "101_at" "1021_at"  
##  
## $`6`  
## [1] "1026_s_at" "1027_at"
```

But look what happens here if we try to unlist that:

```
unlist(mget(chrs, revmap(hgu95av2CHR[1:30]), ifnotfound=NA))  
##          121          122          123          124          61          62  
## "1018_at" "1019_g_at" "101_at" "1021_at" "1026_s_at" "1027_at"
```

Yuck! One trick that will sometimes help is to use `Rfunctionunlist2`. But be careful here too. Depending on what step comes next, `Rfunctionunlist2` may not really help you...

```
unlist2(mget(chrs, revmap(hgu95av2CHR[1:30]), ifnotfound=NA))  
##          12          12          12          12          6          6  
## "1018_at" "1019_g_at" "101_at" "1021_at" "1026_s_at" "1027_at"
```

Lets ask if the probes in 'pbids' mapped to cytogenetic location "18q11.2"?

```
x <- hgu95av2MAP  
pbids <- c("38912_at", "41654_at", "907_at", "2053_at", "2054_g_at",  
          "40781_at")  
x <- subset(x, Lkeys=pbids, Rkeys="18q11.2")  
toTable(x)  
## [1] probe_id          cytogenetic_location  
## <0 rows> (or 0-length row.names)
```

To coerce this map to a named vector:

```
pb2cyto <- as.character(x)  
pb2cyto[pbids]  
## <NA> <NA> <NA> <NA> <NA> <NA>  
## NA NA NA NA NA NA
```

The coercion of the reverse map works too but issues a warning because of the duplicated names for the reasons stated above:

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```
cyto2pb <- as.character(revmap(x))
```

2.0.5 Accessing probes that map to multiple targets

In many probe packages, some probes are known to map to multiple genes. The reasons for this can be biological as happens in the arabidopsis packages, but usually it is due to the fact that the genome builds that chip platforms were based on were less stable than desired. Thus what may have originally been a probe designed to measure one thing can end up measuring many things. Usually you don't want to use probes like this, because if the manufacturer doesn't know what they map to then their usefulness is definitely suspect. For this reason, by default all chip packages will normally hide such probes in the standard mappings. But sometimes you may want access to the answers that the manufacturer says such a probe will map to. In such cases, you will want to use the `toggleProbes` method. To use this method, just call it on a standard mapping and copy the result into a new mapping (you cannot alter the original mapping). Then treat the new mapping as you would any other mapping.

```
## How many probes?
dim(hgu95av2ENTREZID)

## [1] 11471      2

## Make a mapping with multiple probes exposed
multi <- toggleProbes(hgu95av2ENTREZID, "all")
## How many probes?
dim(multi)

## [1] 13426      2
```

If you then decide that you want to make a mapping that has only multiple mappings or you wish to revert one of your maps back to the default state of only showing the single mappings then you can use `toggleProbes` to switch back and forth.

```
## Make a mapping with ONLY multiple probes exposed
multiOnly <- toggleProbes(multi, "multiple")
## How many probes?
dim(multiOnly)

## [1] 1955      2

## Then make a mapping with ONLY single mapping probes
singleOnly <- toggleProbes(multiOnly, "single")
## How many probes?
dim(singleOnly)

## [1] 11471      2
```

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Finally, there are also a pair of test methods `hasMultiProbes` and `hasSingleProbes` that can be used to see what methods a mapping presently has exposed.

```
## Test the multiOnly mapping
hasMultiProbes(multiOnly)

## [1] TRUE

hasSingleProbes(multiOnly)

## [1] FALSE

## Test the singleOnly mapping
hasMultiProbes(singleOnly)

## [1] FALSE

hasSingleProbes(singleOnly)

## [1] TRUE
```

2.0.6 Using SQL to access things directly

While the mapping objects provide a lot of convenience, sometimes there are definite benefits to writing a simple SQL query. But in order to do this, it is necessary to know a few things. The 1st thing you will need to know is some SQL. Fortunately, it is quite easy to learn enough basic SQL to get stuff out of a database. Here are 4 basic SQL things that you may find handy:

First, you need to know about SELECT statements. A simple example would look something like this:

```
SELECT * FROM genes;
```

Which would select everything from the genes table.

```
SELECT gene_id FROM genes;
```

Will select only the gene_id field from the genes table.

Second you need to know about WHERE clauses:

```
SELECT gene_id, _id FROM genes WHERE gene_id=1;
```

Will only get records from the genes table where the gene_id is = 1.

Thirdly, you will want to know about an inner join:

```
SELECT * FROM genes,chromosomes WHERE genes._id=chromosomes._id;
```

This is only slightly more complicated to understand. Here we want to get all the records that are in both the 'genes' and 'chromosomes' tables, but we only want ones where the '_id' field is identical. This is known as an inner join because we only want

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the elements that are in both of these tables with respect to '._id'. There are other kinds of joins that are worth learning about, but most of the time, this is all you will need to do.

Finally, it is worthwhile to learn about the AS keyword which is useful for making long queries easier to read. For the previous example, we could have written it this way to save space:

```
SELECT * FROM genes AS g,chromosomes AS c WHERE g._id=c._id;
```

In a simple example like this you might not see a lot of savings from using AS, so let's consider what happens when we want to also specify which fields we want:

```
SELECT g.gene_id,c.chromosome FROM genes AS g,chromosomes AS c WHERE g._id=c._id;
```

Now you are most of the way there to being able to query the databases directly. The only other thing you need to know is a little bit about how to access these databases from R. With each package, you will also get a method that will print the schema for its database, you can view this to see what sorts of tables are present etc.

```
org.Hs.eg_dbschema()
```

To access the data in a database, you will need to connect to it. Fortunately, each package will automatically give you a connection object to that database when it loads.

```
org.Hs.eg_dbconn()
```

You can use this connection object like this:

```
query <- "SELECT gene_id FROM genes LIMIT 10;"
result = dbGetQuery(org.Hs.eg_dbconn(), query)
result
```

Exercise 5

Retrieve the entrez gene ID and chromosome by using a database query. Show how you could do the same thing by using `toTable`

2.0.7 Combining data from multiple annotation packages at the SQL level

For a more complex example, consider the task of obtaining all gene symbols which are probed on a chip that have at least one GO BP ID annotation with evidence code IMP, IGI, IPI, or IDA. Here is one way to extract this using the environment-based packages:

```
## Obtain SYMBOLS with at least one GO BP
## annotation with evidence IMP, IGI, IPI, or IDA.
system.time({
```

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```
bpids <- eapply(hgu95av2G0, function(x) {
  if (length(x) == 1 && is.na(x))
    NA
  else {
    sapply(x, function(z) {
      if (z$ontology == "BP")
        z$G0ID
      else
        NA
    })
  }
})
bpids <- unlist(bpids)
bpids <- unique(bpids[!is.na(bpids)])
g2p <- mget(bpids, hgu95av2G02PROBE)
wantedp <- lapply(g2p, function(x) {
  x[names(x) %in% c("IMP", "IGI", "IPI", "IDA")]
})
wantedp <- wantedp[sapply(wantedp, length) > 0]
wantedp <- unique(unlist(wantedp))
ans <- unlist(mget(wantedp, hgu95av2SYMBOL))
})
length(ans)
ans[1:10]
```

All of the above code could have been reduced to a single SQL query with the SQLite-based packages. But to put together this query, you would need to look 1st at the schema to know what tables are present:

```
hgu95av2_dbschema()
```

This function will give you an output of all the create table statements that were used to generate the hgu95av2 database. In this case, this is a chip package, so you will also need to see the schema for the organism package that it depends on. To learn what package it depends on, look at the ORGPKG value:

```
hgu95av2ORGPKG
```

Then you can see that schema by looking at its schema method:

```
org.Hs.eg_dbschema()
```

So now we can see that we want to connect the data in the go_bp, and symbol tables from the org.Hs.eg.sqlite database along with the probes data in the hgu95av2.sqlite database. How can we do that?

How to use bimap from the ".db" annotation packages

It turns out that one of the great conveniences of SQLite is that it allows other databases to be 'ATTACHed'. Thus, we can keep our data in many different databases, and then 'ATTACH' them to each other in a modular fashion. The databases for a given build have been built together and frozen into a single version specifically to allow this sort of behavior. To use this feature, the SQLite ATTACH command requires the filename for the database file on your filesystem. Fortunately, R provides a nice system independent way of getting that information. Note that the name of the database is always the same as the name of the package, with the suffix '.sqlite':

```
orgDBLoc = system.file("extdata", "org.Hs.eg.sqlite", package="org.Hs.eg.db")
attachSQL = paste("ATTACH '", orgDBLoc, "' AS orgDB;", sep = "")
dbGetQuery(hgu95av2_dbconn(), attachSQL)

## Warning in rsqlite_fetch(res@ptr, n = n): Don't need to call dbFetch()
## for statements, only for queries

## data frame with 0 columns and 0 rows
```

Finally, you can assemble a cross-db sql query and use the helper function as follows. Note that when we want to refer to tables in the attached database, we have to use the 'orgDB' prefix that we specified in the 'ATTACH' query above.:

```
system.time({
  SQL <- "SELECT DISTINCT probe_id,symbol FROM probes, orgDB.gene_info AS gi, orgDB.genes AS g, orgDB
  zz <- dbGetQuery(hgu95av2_dbconn(), SQL)
})

##      user  system elapsed
## 0.158    0.043    0.202

#its a good idea to always DETACH your database when you are finished...
dbGetQuery(hgu95av2_dbconn(), "DETACH orgDB"
)

## Warning in rsqlite_fetch(res@ptr, n = n): Don't need to call dbFetch()
## for statements, only for queries

## data frame with 0 columns and 0 rows
```

Exercise 6

Retrieve the entrez gene ID, chromosome location information and cytoband information by using a single database query.

Exercise 7

Expand on the example in the text above to combine data from the hgu95av2.db and org.Hs.eg.db with the GO.db package so as to include the GO ID, and term definition in the output.

```
## Warning in rsqlite_fetch(res@ptr, n = n): Don't need to call dbFetch()
## for statements, only for queries
```

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```
## Warning in rsqLite_fetch(res@ptr, n = n): Don't need to call dbFetch()
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```

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

```
## R version 3.4.2 (2017-09-28)
## Platform: x86_64-apple-darwin15.6.0 (64-bit)
## Running under: OS X El Capitan 10.11.6
##
## Matrix products: default
## BLAS: /Library/Frameworks/R.framework/Versions/3.4/Resources/lib/libRblas.0.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/3.4/Resources/lib/libRlapack.dylib
##
## locale:
## [1] C/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## attached base packages:
## [1] parallel stats4      stats      graphics  grDevices utils
## [7] datasets  methods    base
##
## other attached packages:
## [1] G0.db_3.4.2          hgu95av2.db_3.2.3
## [3] AnnotationForge_1.20.0 org.Hs.eg.db_3.4.2
## [5] AnnotationDbi_1.40.0  IRanges_2.12.0
## [7] S4Vectors_0.16.0      Biobase_2.38.0
## [9] BiocGenerics_0.24.0   DBI_0.7
## [11] knitr_1.17
##
## loaded via a namespace (and not attached):
## [1] Rcpp_0.12.13  magrittr_1.5    bit_1.1-12      rlang_0.1.2
## [5] stringr_1.2.0 blob_1.1.0      highr_0.6       tools_3.4.2
## [9] htmltools_0.3.6 yaml_2.1.14     bit64_0.9-7     rprojroot_1.2
## [13] digest_0.6.12 tibble_1.3.4    bitops_1.0-6    RCurl_1.95-4.8
## [17] memoise_1.1.0 evaluate_0.10.1 RSQLite_2.0     rmarkdown_1.6
## [21] stringi_1.1.5 compiler_3.4.2 backports_1.1.1 XML_3.98-1.9
## [25] BiocStyle_2.6.0 pkgconfig_2.0.1
```