

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

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NOTE The 'bimap' interface to annotation resources is not recommend; 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
```

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

## 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, basename, cbind, colnames, dirname, do.call,
##   duplicated, eval, evalq, get, grep, grepl, intersect,
##   is.unsorted, lapply, mapply, match, mget, order, paste, pmax,
##   pmax.int, pmin, pmin.int, rank, rbind, rownames, sapply,
##   setdiff, sort, table, tapply, union, unique, unsplit, 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 objects are masked from 'package:base':
##
##   I, expand.grid, unname

##
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

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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"  "hgu95av2CHRLCEND"
## [9] "hgu95av2ENSEMBL"  "hgu95av2ENSEMBL2PROBE"
## [11] "hgu95av2ENTREZID" "hgu95av2ENZYME"
## [13] "hgu95av2ENZYME2PROBE" "hgu95av2GENENAME"
## [15] "hgu95av2G0"       "hgu95av2G02ALLPROBES"
## [17] "hgu95av2G02PROBE" "hgu95av2MAP"
## [19] "hgu95av2MAPCOUNTS" "hgu95av2MIM"
## [21] "hgu95av2ORGANISM" "hgu95av2ORGPKG"
## [23] "hgu95av2PATH"     "hgu95av2PATH2PROBE"
## [25] "hgu95av2PFAM"     "hgu95av2PMID"
## [27] "hgu95av2PMID2PROBE" "hgu95av2PROSITE"
## [29] "hgu95av2REFSEQ"   "hgu95av2SYMBOL"
## [31] "hgu95av2UNIPROT"  "hgu95av2_dbInfo"
## [33] "hgu95av2_dbconn"  "hgu95av2_dbfile"
## [35] "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.

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] ""
```

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```
## [4] "This package has the following mappings:"
## [5] ""
## [6] "hgu95av2ACCNUM has 12625 mapped keys (of 12625 keys)"
## [7] "hgu95av2ALIAS2PROBE has 37476 mapped keys (of 131663 keys)"
## [8] "hgu95av2CHR has 11683 mapped keys (of 12625 keys)"
## [9] "hgu95av2CHRENGTHS has 595 mapped keys (of 640 keys)"
## [10] "hgu95av2CHRLC has 11637 mapped keys (of 12625 keys)"
## [11] "hgu95av2CHRLCEND has 11637 mapped keys (of 12625 keys)"
## [12] "hgu95av2ENSEMBL has 11609 mapped keys (of 12625 keys)"
## [13] "hgu95av2ENSEMBL2PROBE has 10016 mapped keys (of 38636 keys)"
## [14] "hgu95av2ENTREZID has 11683 mapped keys (of 12625 keys)"
## [15] "hgu95av2ENZYME has 2137 mapped keys (of 12625 keys)"
## [16] "hgu95av2ENZYME2PROBE has 785 mapped keys (of 975 keys)"
## [17] "hgu95av2GENENAME has 11683 mapped keys (of 12625 keys)"
## [18] "hgu95av2G0 has 11475 mapped keys (of 12625 keys)"
## [19] "hgu95av2G02ALLPROBES has 20621 mapped keys (of 22834 keys)"
## [20] "hgu95av2G02PROBE has 15988 mapped keys (of 18644 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] "39758_f_at" "34055_at" "34045_at" "38348_at" "40584_at"
```

The usual ways of accessing annotation data are also available.

```
hgu95av2ENTREZID[[probes[1]]]

## [1] "3916"

hgu95av2ENTREZID$"31882_at"

## [1] "9136"

syms <- unlist(mget(probes, hgu95av2SYMBOL))
syms
```

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```
## 39758_f_at 34055_at 34045_at 38348_at 40584_at
## "LAMP1" "ACVR1B" "CT62" "ACOX2" "NUP88"
```

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.

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)))
```

```
## LAMP1 ACVR1B1 ACVR1B2 ACVR1B3 ACVR1B4
## "39758_f_at" "34055_at" "34056_g_at" "34415_at" "36451_at"
```

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```
##      ACVR1B5      ACVR1B6      CT62      ACOX2      NUP881
## "39199_at" "921_s_at" "34045_at" "38348_at" "40584_at"
##      NUP882
## "40804_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:

```
Term("GO:0000018")
##
##      GO:0000018
```

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```
## "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 34055_at GO:0000082      IDA      BP  
## 2 34055_at GO:0001701      IEA      BP  
## 3 34055_at GO:0001942      IEA      BP  
## 4 34055_at GO:0006355      IDA      BP  
## 5 34055_at GO:0006468      IBA      BP  
## 6 34055_at GO:0006468      IDA      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':

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


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```
## 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
```

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

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`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" "1007_s_at" "1008_f_at" "1009_at"
count.mappedkeys(x)    # nb of mapped keys
## [1] 10
## 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" "1007_s_at" "1008_f_at" "1009_at"
count.mappedLkeys(x)   # nb of mapped Lkeys
## [1] 10
```

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] "1037_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 are not assigned to a chromosome:

```
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
```

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```
## [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  
## 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
```

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```
## 41    1624_at      4
## 42    1629_s_at   4
## 43    1653_at      4
## 44    1670_at     13
## 45    1672_f_at   13
## 46    1679_at      4
## 47    1708_at      4
## 48    1709_g_at   4
## 49     170_at     13
## 50    1720_at      4
## 51    1721_g_at   4
## 52    1731_at      4
## 53    1732_at      4
## 54    1819_at     13
## 55    1828_s_at   4
## 56    1836_at      4
## 57    1883_s_at   4
## 58    1888_s_at   4
## 59    1900_at     13
## 60    1905_s_at   13
## 61    1913_at      4
## 62    1914_at     13
## 63    1931_at     13
## 64    1934_s_at   4
## 65    1943_at      4
## 66    1954_at      4
## 67    1963_at     13
## 68    1964_g_at   13
## 69    1968_g_at   4
## 70    1987_at      4
## 71    1988_at      4
## 72    1989_at     13
## 73    1990_g_at   13
## 74    2044_s_at   13
## 75    2062_at      4
## 76    2092_s_at   4
## 77     214_at      4
## 78    215_g_at     4
## 79     252_at     13
## 80    253_g_at    13
## 81     260_at      4
## 82    281_s_at      4
## 83   31314_at      4
## 84   31320_at     13
## 85   31333_at      4
```

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```
## 86 31345_at 4
## 87 31349_at 4
## 88 31356_at 4
## 89 31382_f_at 4
## 90 31404_at 13
## 91 31408_at 4
## 92 31464_at 13
## 93 31465_g_at 13
## 94 31516_f_at 13
## 95 31543_at 4
## 96 31562_at 13
## 97 31584_at 13
## 98 31628_at 13
## 99 31631_f_at 4
## 100 31639_f_at 13
## 101 31640_r_at 13
## 102 31670_s_at 4
## 103 31684_at 4
## 104 31686_at 4
## 105 31706_at 4
## 106 31744_at 4
## 107 31753_at 13
## 108 31790_at 13
## 109 31792_at 4
## 110 31805_at 4
## 111 31811_r_at 4
## 112 31847_at 13
## 113 31849_at 13
## 114 31851_at 13
## 115 31876_r_at 4
## 116 31894_at 4
## 117 31969_i_at 4
## 118 31970_r_at 4
## 119 32006_r_at 4
## 120 32026_s_at 4
## 121 32080_at 4
## 122 32102_at 13
## 123 32145_at 4
## 124 32146_s_at 4
## 125 32147_at 13
## 126 32148_at 13
## 127 32180_s_at 4
## 128 32220_at 13
## 129 32299_at 4
## 130 32337_at 13
```

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```
## 131 32349_at      4
## 132 32353_at      4
## 133 32357_at      4
## 134 32368_at     13
## 135 32393_s_at    4
## 136 32439_at     13
## 137 32446_at      4
## 138 32449_at      4
## 139 32465_at      4
## 140 32482_at     13
## 141 32506_at      4
## 142 32570_at      4
## 143 32580_at      4
## 144 32595_at      4
## 145 32602_at      4
## 146 32641_at     13
## 147 32675_at      4
## 148 32703_at      4
## 149 32768_at     13
## 150 32769_at      4
## 151 32770_at      4
## 152 32771_at      4
## 153 32812_at      4
## 154 32822_at      4
## 155 32832_at      4
## 156 32862_at     13
## 157 32906_at     13
## 158 32979_at      4
## 159 32986_s_at   13
## 160 32998_at      4
## 161 33013_at      4
## 162 33068_f_at    4
## 163 33069_f_at    4
## 164 33100_at      4
## 165 33150_at      4
## 166 33151_s_at    4
## 167 33155_at      4
## 168 33156_at      4
## 169 33168_at     13
## 170 33171_s_at    4
## 171 33172_at      4
## 172 33173_g_at    4
## 173 33199_at     13
## 174 33208_at     13
## 175 33241_at      4
```

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```
## 176 33249_at      4
## 177 33267_at      4
## 178 33276_at     13
## 179 33299_at      4
## 180 33318_at     13
## 181 33356_at      4
## 182 33359_at      4
## 183 33369_at      4
## 184 33370_r_at    4
## 185 33382_at      4
## 186 33483_at      4
## 187 33488_at      4
## 188 33490_at      4
## 189 33494_at      4
## 190 33519_at      4
## 191 33520_at     13
## 192 33525_at      4
## 193 33526_at      4
## 194 33529_at      4
## 195 33536_at      4
## 196 33544_at      4
## 197 33564_at      4
## 198 33576_at     13
## 199 33584_at      4
## 200 33596_at      4
## 201 33657_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
## 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
```

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```
## 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 34170_s_at    4
## 228 34181_at      4
## 229 34198_at      4
## 230 34211_at     13
## 231 34225_at      4
## 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
## 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
```


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```
## 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
## 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
```

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```
## 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
## 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
```

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```
## 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
## 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
```

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```
## 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 37840_at      4
## 426 37852_at      4
## 427 37926_at      13
## 428 37930_at      13
## 429 37964_at      4
## 430 38008_at      4
## 431 38016_at      4
## 432 38024_at      4
## 433 38025_r_at    4
## 434 38035_at      13
## 435 38065_at      4
## 436 38102_at      13
## 437 38120_at      4
## 438 38168_at      4
## 439 38254_at      4
## 440 38304_r_at    13
## 441 38350_f_at    13
## 442 38353_at      13
## 443 38375_at      13
## 444 38438_at      4
## 445 38485_at      4
```

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```
## 446 38488_s_at      4
## 447 38489_at      4
## 448 38587_at      4
## 449 38606_at      4
## 450 38615_at     13
## 451 38639_at      4
## 452 38643_at      4
## 453 38649_at     13
## 454 38714_at      4
## 455 38715_at      4
## 456 38736_at      4
## 457 38751_i_at     4
## 458 38752_r_at     4
## 459 38767_at      4
## 460 38768_at      4
## 461 38778_at      4
## 462 38821_at      4
## 463 38825_at      4
## 464 38838_at      4
## 465 38854_at      4
## 466 38891_at      4
## 467 38923_at      4
## 468 38957_at     13
## 469 38972_at     13
## 470 38988_at      4
## 471 39028_at     13
## 472 39032_at     13
## 473 39037_at      4
## 474 39056_at      4
## 475 39083_at      4
## 476 39131_at     13
## 477 39132_at      4
## 478 39208_i_at     4
## 479 39209_r_at     4
## 480 39224_at      4
## 481 39256_at     13
## 482 39257_at     13
## 483 39269_at     13
## 484 39295_s_at     4
## 485 39333_at     13
## 486 39337_at      4
## 487 39355_at      4
## 488 39369_at      4
## 489 39380_at      4
## 490 39382_at      4
```

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```
## 491 39405_at      13
## 492 39469_s_at    13
## 493 39475_at      4
## 494 39481_at      4
## 495 39488_at      13
## 496 39489_g_at    13
## 497 39535_at      4
## 498 39554_at      4
## 499 39555_at      4
## 500 39576_at      4
## 501 39579_at     13
## 502 39600_at      4
## 503 39634_at      4
## 504 39662_s_at    4
## 505 39665_at      4
## 506 39680_at      4
## 507 39690_at      4
## 508 39698_at      4
## 509 39734_at      4
## 510 39746_at      4
## 511 39748_at     13
## 512 39758_f_at    13
## 513 39777_at     13
## 514 39786_at      4
## 515 39847_at      4
## 516 39850_at      4
## 517 39851_at      4
## 518 39852_at     13
## 519 39878_at     13
## 520 39897_at      4
## 521 39924_at     13
## 522 39929_at      4
## 523 39955_at     13
## 524 39960_at      4
## 525 39979_at     13
## 526 40018_at     13
## 527 40058_s_at    4
## 528 40059_r_at    4
## 529 40060_r_at    4
## 530 40067_at     13
## 531 40072_at     13
## 532 40082_at      4
## 533 400_at        13
## 534 40114_at      4
## 535 40121_at      4
```

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```
## 536 40148_at      4
## 537 40180_at     13
## 538 40181_f_at   13
## 539 40199_at      4
## 540 40217_s_at    4
## 541 40218_at      4
## 542 40225_at      4
## 543 40226_at      4
## 544 40272_at      4
## 545 40310_at      4
## 546 40312_at     13
## 547 40323_at      4
## 548 40349_at      4
## 549 40354_at      4
## 550 40392_at     13
## 551 40404_s_at   13
## 552 40449_at      4
## 553 40454_at      4
## 554 40456_at      4
## 555 40473_at     13
## 556 40492_at      4
## 557 40530_at      4
## 558 40570_at     13
## 559 40576_f_at    4
## 560 40633_at     13
## 561 40681_at     13
## 562 40697_at      4
## 563 40710_at      4
## 564 40711_at      4
## 565 40727_at      4
## 566 40746_at      4
## 567 40770_f_at    4
## 568 40772_at      4
## 569 40773_at      4
## 570 40818_at      4
## 571 40828_at     13
## 572 40839_at     13
## 573 40853_at      4
## 574 40880_r_at    4
## 575 40893_at     13
## 576 408_at        4
## 577 40908_r_at   13
## 578 40943_at      4
## 579 40970_at     13
## 580 40990_at      4
```

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```
## 581 40991_at 4
## 582 40992_s_at 4
## 583 40993_r_at 4
## 584 41014_s_at 4
## 585 41024_f_at 4
## 586 41025_r_at 4
## 587 41026_f_at 4
## 588 41069_at 13
## 589 41071_at 4
## 590 41104_at 4
## 591 41118_at 13
## 592 41119_f_at 13
## 593 41145_at 4
## 594 41148_at 4
## 595 41182_at 13
## 596 41191_at 4
## 597 41276_at 13
## 598 41277_at 13
## 599 41300_s_at 13
## 600 41301_at 13
## 601 41308_at 4
## 602 41309_g_at 4
## 603 41317_at 13
## 604 41318_g_at 13
## 605 41319_at 13
## 606 41376_i_at 4
## 607 41377_f_at 4
## 608 41391_at 4
## 609 41392_at 4
## 610 41402_at 4
## 611 41434_at 4
## 612 41436_at 13
## 613 41456_at 4
## 614 41459_at 13
## 615 41470_at 4
## 616 41491_s_at 13
## 617 41492_r_at 13
## 618 41493_at 13
## 619 41534_at 4
## 620 41555_at 4
## 621 41556_s_at 4
## 622 41585_at 4
## 623 41667_s_at 13
## 624 41668_r_at 13
## 625 41697_at 4
```


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```
## 626 41801_at      4
## 627 41806_at      4
## 628 41860_at     13
## 629   431_at      4
## 630   504_at      4
## 631 507_s_at      4
## 632   579_at      4
## 633   618_at      4
## 634   630_at      4
## 635 631_g_at      4
## 636   655_at      4
## 637 690_s_at      4
## 638 692_s_at      4
## 639 764_s_at      4
## 640   820_at      4
## 641   886_at      4
## 642   931_at     13
## 643 936_s_at      4
## 644 948_s_at      4
## 645   963_at     13
## 646   975_at      4
## 647   990_at     13
## 648 991_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)

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

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```
## [1] "1007_s_at" "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" "1007_s_at" "1026_s_at"  
##          63  
## "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" "1007_s_at" "1026_s_at"  
##          6  
## "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 they 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] 11683    2  
  
## Make a mapping with multiple probes exposed  
multi <- toggleProbes(hgu95av2ENTREZID, "all")  
## How many probes?  
dim(multi)  
## [1] 12981    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] 1298    2  
  
## Then make a mapping with ONLY single mapping probes  
singleOnly <- toggleProbes(multiOnly, "single")  
## How many probes?  
dim(singleOnly)  
## [1] 11683    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 lets 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({
  bpidb <- eapply(hgu95av2G0, function(x) {
```

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```
if (length(x) == 1 && is.na(x))
  NA
else {
  sapply(x, function(z) {
    if (z$ontology == "BP")
      z$GOID
    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?

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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 result_fetch(res@ptr, n = n): SQL statements must be issued
with dbExecute() or dbSendStatement() instead of dbGetQuery() or dbSendQuery().

## 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
## 0.098   0.033   0.130

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

## Warning in result_fetch(res@ptr, n = n): SQL statements must be issued
with dbExecute() or dbSendStatement() instead of dbGetQuery() or dbSendQuery().

## 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 result_fetch(res@ptr, n = n): SQL statements must be issued
with dbExecute() or dbSendStatement() instead of dbGetQuery() or dbSendQuery().
```

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

```
## Warning in result_fetch(res@ptr, n = n): SQL statements must be issued
with dbExecute() or dbSendStatement() instead of dbGetQuery() or dbSendQuery().

## Warning in result_fetch(res@ptr, n = n): SQL statements must be issued
with dbExecute() or dbSendStatement() instead of dbGetQuery() or dbSendQuery().

## Warning in result_fetch(res@ptr, n = n): SQL statements must be issued
with dbExecute() or dbSendStatement() instead of dbGetQuery() or dbSendQuery().
```

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

```
## R version 4.2.0 RC (2022-04-21 r82226)
## Platform: x86_64-pc-linux-gnu (64-bit)
## Running under: Ubuntu 20.04.4 LTS
##
## Matrix products: default
## BLAS: /home/biocbuild/bbs-3.16-bioc/R/lib/libRblas.so
## LAPACK: /home/biocbuild/bbs-3.16-bioc/R/lib/libRlapack.so
##
## locale:
## [1] LC_CTYPE=en_US.UTF-8 LC_NUMERIC=C
## [3] LC_TIME=en_GB LC_COLLATE=C
## [5] LC_MONETARY=en_US.UTF-8 LC_MESSAGES=en_US.UTF-8
## [7] LC_PAPER=en_US.UTF-8 LC_NAME=C
## [9] LC_ADDRESS=C LC_TELEPHONE=C
## [11] LC_MEASUREMENT=en_US.UTF-8 LC_IDENTIFICATION=C
##
## attached base packages:
## [1] stats4 stats graphics grDevices utils datasets
## [7] methods base
##
## other attached packages:
## [1] hgu95av2.db_3.13.0 AnnotationForge_1.39.0
## [3] org.Hs.eg.db_3.15.0 AnnotationDbi_1.59.1
## [5] IRanges_2.31.0 S4Vectors_0.35.0
## [7] Biobase_2.57.1 BiocGenerics_0.43.0
## [9] DBI_1.1.2 knitr_1.39
##
## loaded via a namespace (and not attached):
## [1] Rcpp_1.0.8.3 XVector_0.37.0
## [3] compiler_4.2.0 BiocManager_1.30.18
## [5] highr_0.9 GenomeInfoDb_1.33.3
## [7] zlibbioc_1.43.0 bitops_1.0-7
## [9] tools_4.2.0 digest_0.6.29
## [11] bit_4.0.4 RSQLite_2.2.14
```


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

```
## [13] evaluate_0.15          memoise_2.0.1
## [15] pkgconfig_2.0.3       png_0.1-7
## [17] rlang_1.0.2           cli_3.3.0
## [19] yaml_2.3.5            xfun_0.31
## [21] fastmap_1.1.0         GenomeInfoDbData_1.2.8
## [23] stringr_1.4.0         httr_1.4.3
## [25] Biostrings_2.65.0     vctrs_0.4.1
## [27] bit64_4.0.5           R6_2.5.1
## [29] XML_3.99-0.9          rmarkdown_2.14
## [31] GO.db_3.15.0          blob_1.2.3
## [33] magrittr_2.0.3        htmltools_0.5.2
## [35] KEGGREST_1.37.0       BiocStyle_2.25.0
## [37] stringi_1.7.6         RCurl_1.98-1.6
## [39] cachem_1.0.6          crayon_1.5.1
```