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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 theses 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.

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
```

```
##
## 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, 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,
##
##
      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
##
## Attaching package: 'IRanges'
## The following object is masked from 'package:grDevices':
##
##
      windows
##
```

```
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] "hqu95av2ACCNUM"
                                 "hgu95av2ALIAS2PR0BE"
    [5] "hgu95av2CHR"
                                 "hgu95av2CHRLENGTHS"
    [7] "hgu95av2CHRL0C"
                                 "hgu95av2CHRL0CEND"
##
   [9] "hgu95av2ENSEMBL"
                                 "hgu95av2ENSEMBL2PR0BE"
##
## [11] "hgu95av2ENTREZID"
                                 "hgu95av2ENZYME"
## [13] "hgu95av2ENZYME2PR0BE"
                                 "hgu95av2GENENAME"
## [15] "hgu95av2G0"
                                 "hgu95av2G02ALLPR0BES"
## [17] "hgu95av2G02PR0BE"
                                 "hgu95av2MAP"
## [19] "hgu95av2MAPCOUNTS"
                                 "hgu95av20MIM"
## [21] "hqu95av20RGANISM"
                                 "hgu95av20RGPKG"
## [23] "hgu95av2PATH"
                                 "hgu95av2PATH2PR0BE"
## [25] "hgu95av2PFAM"
                                 "hgu95av2PMID"
## [27] "hgu95av2PMID2PR0BE"
                                 "hgu95av2PR0SITE"
## [29] "hgu95av2REFSEQ"
                                 "hgu95av2SYMB0L"
## [31] "hgu95av2UNIGENE"
                                 "hgu95av2UNIPROT"
                                 "hgu95av2_dbconn"
## [33] "hgu95av2_dbInfo"
## [35] "hgu95av2_dbfile"
                                 "hgu95av2_dbschema"
```

Exercise 1

Start an R session and use the <u>library</u> function to load the hgu95av2.db software package. Use search() to see that an organism package was also loaded and then use the approriate "_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] ""
##
   [4] "This package has the following mappings:"
## [5] ""
## [6] "hgu95av2ACCNUM has 12625 mapped keys (of 12625 keys)"
## [7] "hqu95av2ALIAS2PR0BE has 34238 mapped keys (of 124119 keys)"
## [8] "hgu95av2CHR has 11472 mapped keys (of 12625 keys)"
## [9] "hgu95av2CHRLENGTHS has 93 mapped keys (of 595 keys)"
## [10] "hgu95av2CHRLOC has 11423 mapped keys (of 12625 keys)"
## [11] "hqu95av2CHRLOCEND has 11423 mapped keys (of 12625 keys)"
## [12] "hgu95av2ENSEMBL has 11365 mapped keys (of 12625 keys)"
## [13] "hgu95av2ENSEMBL2PR0BE has 9545 mapped keys (of 28694 keys)"
## [14] "hgu95av2ENTREZID has 11474 mapped keys (of 12625 keys)"
## [15] "hgu95av2ENZYME has 2097 mapped keys (of 12625 keys)"
## [16] "hgu95av2ENZYME2PR0BE 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] "hgu95av2G02ALLPR0BES has 18521 mapped keys (of 22272 keys)"
## [20] "hgu95av2G02PR0BE has 13971 mapped keys (of 17496 keys)"
```

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

```
hgu95av2MAPC0UNTS
```

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)</pre>
```

```
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))</pre>
syms
## 39758_f_at
                 34055_at
                             34045_at
                                         38348_at
                                                     40584_at
##
      "LAMP1"
                 "ACVR1B"
                               "CT62"
                                          "AC0X2"
                                                      "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.

?hgu95av2CHRL0C

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
                                                                ACVR1B4
                                    ACVR1B2
                                                 ACVR1B3
## "39758_f_at"
                   "34055_at" "34056_g_at"
                                               "34415_at"
                                                            "36451_at"
##
        ACVR1B5
                      ACVR1B6
                                       CT62
                                                    AC0X2
                                                                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"</pre>
```

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:

```
##

## G0:0000018

## "regulation of DNA recombination"

Definition("G0:0000018")

##

## "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.

Term("G0:0000018")

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 G0:0000082
                                          BP
                               IDA
## 2 34055_at G0:0001701
                               IEA
                                          BP
## 3 34055_at G0:0001942
                               IEA
                                          BP
## 4 34055_at G0:0006355
                               IDA
                                          BP
## 5 34055_at G0:0006468
                               IDA
                                          BP
## 6 34055_at G0:0007165
                               TDA
                                          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 is 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
## 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)</pre>
```

There are more 'undirected' methods listed below:

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. Similarily, 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 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 \leftarrow Rkeys(x)[23:24]
chroms
## [1] "4" "13"
Rkeys(x) <- chroms</pre>
toTable(x)
##
        probe_id chromosome
## 1
       1029_s_at
## 2
        1036_at
                        4
## 3
        1058_at
                       13
## 4
        1065_at
                       13
## 5
        1115_at
                       4
## 6
        1189_at
                       13
## 7
                       13
        1198_at
## 8
        1219_at
                       4
## 9
      1220_g_at
                        4
## 10
        1249_at
## 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_q_at
                        4
## 18
      1451_s_at
                       13
## 19
       1503_at
                       13
      1507_s_at
                        4
## 20
## 21
      1527_s_at
                       13
## 22
       1528_at
                       13
## 23
        1529_at
                       13
## 24
                       13
      1530_g_at
## 25
       1531_at
                       13
## 26
      1532_g_at
                       13
## 27
      1538_s_at
                        4
## 28
        1542_at
```

```
## 29
                        13
       1545_g_at
## 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
## 38
        1604_at
                        4
## 39
       1605_g_at
                        4
## 40
       1616_at
                        13
## 41
        1624_at
                        4
## 42
                        4
      1629_s_at
## 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
                        4
       1883_s_at
## 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
                        4
## 63
      1934_s_at
## 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
                         4
## 73
         2062_at
```

```
## 74
       2092_s_at
                       4
       214_at
## 75
                      4
## 76
      215_g_at
                      4
## 77
       252_at
                      13
## 78
       253_g_at
                      13
## 79
       260_at
                     4
## 80
                      4
      281_s_at
## 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
## 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
## 123 32148_at
                      13
## 124 32163_f_at
                     4
## 125 32180_s_at
                      4
## 126 32220_at
                      13
## 127 32299_at
## 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
## 135 32449_at
                      4
## 136 32465_at
                      4
## 137 32482_at
                      13
## 138 32506_at
                     4
## 139 32507_at
                      4
## 140 32570_at
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## 167 33168_at
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## 168 33171_s_at
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## 233 34240_s_at
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## 329 35871_s_at
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## 330
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## 332 35939_s_at
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## 402 37322_s_at
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## 524 40059_r_at
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## 557 40681_at
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## 570 40880_r_at
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## 571 40893_at
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## 573 40908_r_at
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## 574 40943_at
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## 575 40970_at
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## 576 40989_at
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## 577 40990_at
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## 579 40992_s_at
## 580 40993_r_at
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## 581 41014_s_at
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## 582 41024_f_at
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## 584 41026_f_at
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## 619 41585_at
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## 620 41667_s_at
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## 621 41668_r_at
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## 622 41697_at
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## 623 41801_at
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## 624 41806_at
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## 625 41860_at
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## 626 431_at
## 627 504_at
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## 628 507_s_at
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## 629 579_at
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      618_at
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## 631 630_at
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## 632 631_g_at
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## 633 655_at
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## 634 690_s_at
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## 635 692_s_at
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## 636 764_s_at
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## 637 820_at
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## 638 886_at
## 639 931_at
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                      13
## 640 936_s_at
                      4
## 641 948_s_at
                       4
      963_at
## 642
                      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</pre>
```

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`
## [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"?

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
```

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

```
cyto2pb <- as.character(revmap(x))</pre>
```

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 usefullness 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] 11460    2

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

## [1] 13395    2</pre>
```

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.

```
## [1] 11460       2
```

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 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</pre>
```

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({
bpids <- eapply(hgu95av2G0, function(x) {</pre>
    if (length(x) == 1 \&\& is.na(x))
      NA
    else {
        sapply(x, function(z) {
             if (z$0ntology == "BP")
               z$GOID
             else
               NA
             })
    }
})
bpids <- unlist(bpids)</pre>
bpids <- unique(bpids[!is.na(bpids)])</pre>
g2p <- mget(bpids, hgu95av2G02PR0BE)</pre>
wantedp <- lapply(g2p, function(x) {</pre>
    x[names(x) %in% c("IMP", "IGI", "IPI", "IDA")]
})
wantedp <- wantedp[sapply(wantedp, length) > 0]
wantedp <- unique(unlist(wantedp))</pre>
ans <- unlist(mget(wantedp, hgu95av2SYMBOL))</pre>
})
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:

```
hgu95av20RGPKG
```

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?

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 differnt 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 behavoir. 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
## 0.19 0.14 0.42

#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</pre>
```

Exercise 6

Retrieve the entrez gene ID, chromosome location information and cytoband infomration 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().

## 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 3.6.1 (2019-07-05)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows Server 2012 R2 x64 (build 9600)
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=C
## [2] LC_CTYPE=English_United States.1252
## [3] LC_MONETARY=English_United States.1252
## [4] LC_NUMERIC=C
## [5] LC_TIME=English_United States.1252
##
## attached base packages:
## [1] parallel stats4
                                    graphics grDevices utils
                          stats
## [7] datasets methods
                          base
##
## other attached packages:
## [1] hgu95av2.db_3.2.3
                              AnnotationForge_1.26.0
## [3] org.Hs.eg.db_3.8.2
                              AnnotationDbi_1.46.1
## [5] IRanges_2.18.1
                              S4Vectors_0.22.0
##
   [7] Biobase_2.44.0
                              BiocGenerics_0.30.0
   [9] DBI_1.0.0
                              knitr_{-}1.24
##
##
## loaded via a namespace (and not attached):
## [1] Rcpp_1.0.2
                          compiler_3.6.1
                                             pillar_1.4.2
## [4] BiocManager_1.30.4 highr_0.8
                                             bitops_1.0-6
## [7] tools_3.6.1
                        zeallot_0.1.0
                                             digest_0.6.20
```

```
## [10] bit_1.1-14
                          RSQLite_2.1.2
                                             evaluate_0.14
## [13] memoise_1.1.0
                          tibble_2.1.3
                                             pkgconfig_2.0.2
## [16] rlang_0.4.0
                          yaml_2.2.0
                                             xfun_0.8
## [19] stringr_1.4.0
                          vctrs_0.2.0
                                             bit64_0.9-7
## [22] XML_3.98-1.20
                          rmarkdown_1.14
                                             G0.db_3.8.2
## [25] blob_1.2.0
                          magrittr_1.5
                                             backports_1.1.4
## [28] htmltools_0.3.6
                          BiocStyle_2.12.0
                                             stringi_1.4.3
## [31] RCurl_1.95-4.12
                          crayon_1.3.4
```