

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

Marc Carlson, Herve Pages, Seth Falcon, Nianhua Li

December 8, 2015

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.

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(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, xtabs
##
## The following objects are masked from 'package:base':
##
##   Filter, Find, Map, Position, Reduce, anyDuplicated, append, as.data.frame,
##   as.vector, cbind, 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, rownames, sapply,
##   setdiff, sort, table, tapply, union, unique, unlist, unsplit
##
## 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
## Loading required package: DBI

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

2 Examples

2.0.4 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] "hgu95av2GO"             "hgu95av2GO2ALLPROBES"
## [17] "hgu95av2GO2PROBE"       "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.

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 118097 keys)"
## [8] "hgu95av2CHR has 11472 mapped keys (of 12625 keys)"
## [9] "hgu95av2CHRLNGTHS has 93 mapped keys (of 93 keys)"
## [10] "hgu95av2CHRLOC has 11423 mapped keys (of 12625 keys)"
## [11] "hgu95av2CHRLOCEND has 11423 mapped keys (of 12625 keys)"
## [12] "hgu95av2ENSEMBL has 11365 mapped keys (of 12625 keys)"
## [13] "hgu95av2ENSEMBL2PROBE has 9545 mapped keys (of 30486 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] "hgu95av2GO has 11229 mapped keys (of 12625 keys)"
## [19] "hgu95av2GO2ALLPROBES has 18521 mapped keys (of 20246 keys)"
## [20] "hgu95av2GO2PROBE has 13971 mapped keys (of 15895 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.

```
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.

2.0.5 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)))
##      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] "35870_at" "36132_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] "35870_at" "36132_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")

## 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 metaboli
```

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.

2.0.6 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:0000186      TAS      BP
## 3  1702_at  GO:0002437      IEA      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':

```
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
```

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.

2.0.7 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

## [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
## 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
## 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
## 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
```

```
## 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
## 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
##	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
## 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
## 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
##	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
## 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
## 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
## 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
## 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
## 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)

## $`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)
##      probe_id cytogenetic_location
## 1    2053_at                18q11.2
## 2  2054_g_at                18q11.2
```

To coerce this map to a named vector:

```
pb2cyto <- as.character(x)
pb2cyto[pbids]
##      <NA>      <NA>      <NA>    2053_at 2054_g_at      <NA>
##      NA      NA      NA  "18q11.2" "18q11.2"      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))
## Warning in .local(x, ...): returned vector has duplicated names
```

2.0.8 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] 11474      2

## Make a mapping with multiple probes exposed
multi <- toggleProbes(hgu95av2ENTREZID, "all")
## How many probes?
dim(multi)
## [1] 13447      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] 1973    2

## Then make a mapping with ONLY single mapping probes
singleOnly <- toggleProbes(multiOnly, "single")
## How many probes?
dim(singleOnly)
## [1] 11474    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
```

2.0.9 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 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

2.0.10 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({
bpidids <- eapply(hgu95av2G0, function(x) {
  if (length(x) == 1 && is.na(x))
    NA
  else {
    sapply(x, function(z) {
```

```

        if (z$Ontology == "BP")
          z$GOID
        else
          NA
      })
    }
  })
bpid <- unlist(bpids)
bpid <- unique(bpid[!is.na(bpid)])
g2p <- mget(bpid, hgu95av2G02PROBE)
wanted <- lapply(g2p, function(x) {
  x[names(x) %in% c("IMP", "IGI", "IPI", "IDA")]
})
wanted <- wanted[sapply(wanted, length) > 0]
wanted <- unique(unlist(wanted))
ans <- unlist(mget(wanted, 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?

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)

```

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, org
zz <- dbGetQuery(hgu95av2_dbconn(), SQL)
})

##      user  system elapsed
## 0.241   0.004   0.257

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

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.

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

```
## R version 3.2.2 (2015-08-14)
## Platform: x86_64-pc-linux-gnu (64-bit)
## Running under: Ubuntu 14.04.3 LTS
##
## locale:
##  [1] LC_CTYPE=en_US.UTF-8      LC_NUMERIC=C
##  [3] LC_TIME=en_US.UTF-8      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] parallel stats4 stats graphics grDevices utils
## [7] datasets methods base
##
## other attached packages:
##  [1] GO.db_3.2.2             hgu95av2.db_3.2.2
##  [3] AnnotationForge_1.12.1 org.Hs.eg.db_3.2.3
##  [5] RSQLite_1.0.0           DBI_0.3.1
##  [7] AnnotationDbi_1.32.2    IRanges_2.4.5
##  [9] S4Vectors_0.8.4         Biobase_2.30.0
## [11] BiocGenerics_0.16.1     knitr_1.11
##
## loaded via a namespace (and not attached):
## [1] formatR_1.2.1  magrittr_1.5    evaluate_0.8    highr_0.5.1
```

```
## [5] stringi_1.0-1 BiocStyle_1.8.0 tools_3.2.2 stringr_1.0.0
```