

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

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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.

```
> require(org.Hs.eg.db)
```

```
> require(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.

```
R> library("hgu95av2.db")
```

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

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

 [1] "hgu95av2"                "hgu95av2.db"
 [3] "hgu95av2ACCCNUM"        "hgu95av2ALIAS2PROBE"
 [5] "hgu95av2CHR"           "hgu95av2CHRLNGTHS"
 [7] "hgu95av2CHRLOC"        "hgu95av2CHRLOCEND"
 [9] "hgu95av2ENSEMBL"       "hgu95av2ENSEMBL2PROBE"
[11] "hgu95av2ENTREZID"      "hgu95av2ENZYME"
[13] "hgu95av2ENZYME2PROBE"  "hgu95av2GENENAME"
[15] "hgu95av2G0"            "hgu95av2G02ALLPROBES"
[17] "hgu95av2G02PROBE"     "hgu95av2MAP"
[19] "hgu95av2MAPCOUNTS"   "hgu95av2OMIM"
[21] "hgu95av2ORGANISM"     "hgu95av2ORGPKG"
[23] "hgu95av2PATH"         "hgu95av2PATH2PROBE"
[25] "hgu95av2PFAM"         "hgu95av2PMID"
[27] "hgu95av2PMID2PROBE"   "hgu95av2PROSITE"
[29] "hgu95av2REFSEQ"       "hgu95av2SYMBOL"
[31] "hgu95av2UNIGENE"     "hgu95av2UNIPROT"
[33] "hgu95av2_dbInfo"      "hgu95av2_dbconn"
[35] "hgu95av2_dbfile"     "hgu95av2_dbschema"
```

Exercise 1

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

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

```
R> qcdata = capture.output(hgu95av2())
R> 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 33097 mapped keys (of 94889 keys)"
[8] "hgu95av2CHR has 11771 mapped keys (of 12625 keys)"
[9] "hgu95av2CHRLNGTHS has 93 mapped keys (of 93 keys)"
[10] "hgu95av2CHRLLOC has 11715 mapped keys (of 12625 keys)"
[11] "hgu95av2CHRLLOCEND has 11715 mapped keys (of 12625 keys)"
[12] "hgu95av2ENSEMBL has 11647 mapped keys (of 12625 keys)"
[13] "hgu95av2ENSEMBL2PROBE has 9677 mapped keys (of 25527 keys)"
[14] "hgu95av2ENTREZID has 11774 mapped keys (of 12625 keys)"
[15] "hgu95av2ENZYME has 2154 mapped keys (of 12625 keys)"
[16] "hgu95av2ENZYME2PROBE has 791 mapped keys (of 975 keys)"
[17] "hgu95av2GENENAME has 11774 mapped keys (of 12625 keys)"
[18] "hgu95av2G0 has 11395 mapped keys (of 12625 keys)"
[19] "hgu95av2G02ALLPROBES has 15213 mapped keys (of 16527 keys)"
[20] "hgu95av2G02PROBE has 11388 mapped keys (of 12818 keys)"
```

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

```
R> hgu95av2MAPCOUNTS
```

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

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

```
[1] 12625

R> set.seed(Oxa1beef)
R> probes <- sample(all_probes, 5)
R> probes

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

The usual ways of accessing annotation data are also available.

```
R> hgu95av2ENTREZID[[probes[1]]]

[1] "9136"

R> hgu95av2ENTREZID$"31882_at"

[1] "9136"

R> syms <- unlist(mget(probes, hgu95av2SYMBOL))
R> 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.

```
R> ?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.

```
R> system.time(as.list(hgu95av2SYMBOL)[1:10])
R> ## vs:
R>
R> 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.

```
R> 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:

```
R> 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:

```
R> x <- hgu95av2PATH
R> ## except for the name, this is exactly revmap(x)
R> revx <- hgu95av2PATH2PROBE
R> revx2 <- revmap(x, objName="PATH2PROBE")
R> revx2
```

```
PATH2PROBE map for chip hgu95av2 (object of class "ProbeAnnDbBimap")
```

```
R> identical(revx, revx2)
```

```
[1] TRUE
```

```
R> 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:

```
R> Term("GO:0000018")
```

```
GO:0000018
```

```
"regulation of DNA recombination"
```

```
R> Definition("GO:0000018")
```

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

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`.

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

	probe_id	go_id	Evidence	Ontology
1	1702_at	GO:0002437	IEA	BP
2	1702_at	GO:0006915	TAS	BP
3	1702_at	GO:0006924	IEA	BP
4	1702_at	GO:0006955	TAS	BP
5	1702_at	GO:0007166	TAS	BP
6	1702_at	GO:0007219	IEA	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':

```
R> 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

```
R> 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

There can be more than 2 columns in the returned data frame:
3 cols:

```
R> toTable(hgu95av2PFAM)[1:6, ] # the right values are tagged
```

```

      probe_id      ipi_id PfamId
1 1000_at IPI00018195 PF00069
2 1000_at IPI00984821 PF00069
3 1001_at IPI00019530 PF00041
4 1001_at IPI00019530 PF07714
5 1002_f_at IPI00013323 PF00067
6 1003_s_at IPI00027955 PF00001

```

```
R> as.list(hgu95av2PFAM["1000_at"])
```

```

$`1000_at`
IPI00018195 IPI00984821
"PF00069" "PF00069"

```

But the Rkeys are ALWAYS in the 2nd col.

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

```
R> length(x)
```

```
[1] 12625
```

```
R> length(revx)
```

```
[1] 229
```

```
R> allProbeSetIds <- keys(x)
```

```
R> allKEGGIds <- keys(revx)
```

There are more 'undirected' methods listed below:

```
R> junk <- Lkeys(x)      # same for all maps in hgu95av2.db (except pseudo-map
R>                               # MAPCOUNTS)
R> Llength(x)           # nb of Lkeys
```

```
[1] 12625
```

```
R> junk <- Rkeys(x)      # KEGG ids for PATH/PATH2PROBE maps, GO ids for
R>                               # GO/GO2PROBE/GO2ALLPROBES maps, etc...
R> 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.

```
R> x = hgu95av2ENTREZID[1:10]
R> ## Directed methods
R> 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"
```

```
R> count.mappedkeys(x)   # nb of mapped keys
```

```
[1] 10
```

```
R> ## Undirected methods
R> 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"
```

```
R> 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`.

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

```
[1] "1047_s_at" "1089_i_at" "108_g_at" "1090_f_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:

```
R> x <- hgu95av2CHR
R> 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"
```

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

```
[1] "4" "13"
```

```
R> Rkeys(x) <- chroms
R> 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	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	1987_at	4
70	1988_at	4
71	1989_at	13
72	1990_g_at	13
73	2044_s_at	13
74	2062_at	4
75	2063_at	13
76	2064_g_at	13
77	2092_s_at	4
78	214_at	4
79	215_g_at	4
80	252_at	13
81	253_g_at	13
82	260_at	4
83	281_s_at	4
84	31314_at	4
85	31320_at	13

86	31333_at	4
87	31345_at	4
88	31348_at	4
89	31349_at	4
90	31356_at	4
91	31382_f_at	4
92	31387_at	4
93	31404_at	13
94	31408_at	4
95	31464_at	13
96	31465_g_at	13
97	31516_f_at	13
98	31543_at	4
99	31562_at	13
100	31584_at	13
101	31628_at	13
102	31631_f_at	4
103	31639_f_at	13
104	31640_r_at	13
105	31670_s_at	4
106	31684_at	4
107	31686_at	4
108	31706_at	4
109	31744_at	4
110	31753_at	13
111	31790_at	13
112	31792_at	4
113	31805_at	4
114	31811_r_at	4
115	31847_at	13
116	31849_at	13
117	31851_at	13
118	31876_r_at	4
119	31894_at	4
120	31969_i_at	4
121	31970_r_at	4
122	32006_r_at	4
123	32026_s_at	4
124	32080_at	4
125	32102_at	13

126	32145_at	4
127	32146_s_at	4
128	32147_at	13
129	32148_at	13
130	32180_s_at	4
131	32220_at	13
132	32299_at	4
133	32337_at	13
134	32349_at	4
135	32353_at	4
136	32357_at	4
137	32368_at	13
138	32393_s_at	4
139	32439_at	13
140	32446_at	4
141	32449_at	4
142	32465_at	4
143	32482_at	13
144	32506_at	4
145	32507_at	4
146	32570_at	4
147	32580_at	4
148	32595_at	4
149	32602_at	4
150	32641_at	13
151	32675_at	4
152	32703_at	4
153	32768_at	13
154	32769_at	4
155	32770_at	4
156	32771_at	4
157	32812_at	4
158	32822_at	4
159	32832_at	4
160	32862_at	13
161	32906_at	13
162	32979_at	4
163	32986_s_at	13
164	32998_at	4
165	33013_at	4

166	33050_at	4
167	33068_f_at	4
168	33069_f_at	4
169	33100_at	4
170	33150_at	4
171	33151_s_at	4
172	33155_at	4
173	33156_at	4
174	33168_at	13
175	33171_s_at	4
176	33172_at	4
177	33173_g_at	4
178	33199_at	13
179	33208_at	13
180	33241_at	4
181	33249_at	4
182	33267_at	4
183	33276_at	13
184	33299_at	4
185	33318_at	13
186	33356_at	4
187	33359_at	4
188	33369_at	4
189	33370_r_at	4
190	33382_at	4
191	33483_at	4
192	33488_at	4
193	33490_at	4
194	33494_at	4
195	33519_at	4
196	33520_at	13
197	33525_at	4
198	33526_at	4
199	33529_at	4
200	33536_at	4
201	33544_at	4
202	33564_at	4
203	33576_at	13
204	33584_at	4
205	33596_at	4

206	33657_at	4
207	33672_f_at	4
208	33673_r_at	4
209	33687_at	13
210	33700_at	13
211	33733_at	4
212	33791_at	13
213	33823_at	4
214	33827_at	13
215	33837_at	4
216	33859_at	13
217	33975_at	4
218	33990_at	4
219	33991_g_at	4
220	33992_at	4
221	33997_at	4
222	34021_at	4
223	34022_at	4
224	34026_at	13
225	34029_at	4
226	34048_at	4
227	34051_at	13
228	34058_at	4
229	34075_at	4
230	34122_at	4
231	34131_at	4
232	34144_at	4
233	34145_at	4
234	34149_at	4
235	34170_s_at	4
236	34181_at	4
237	34198_at	4
238	34211_at	13
239	34225_at	4
240	34239_at	13
241	34240_s_at	13
242	34247_at	4
243	34248_at	4
244	34275_s_at	4
245	34284_at	13

246	34307_at	13
247	34319_at	4
248	34324_at	13
249	34334_at	13
250	34335_at	13
251	34341_at	4
252	34342_s_at	4
253	34353_at	4
254	34398_at	13
255	34411_at	4
256	34423_at	4
257	34459_at	13
258	34476_r_at	4
259	34482_at	4
260	34512_at	4
261	34551_at	4
262	34564_at	4
263	34565_at	4
264	34578_at	13
265	34583_at	13
266	34596_at	4
267	34637_f_at	4
268	34638_r_at	4
269	34657_at	13
270	34672_at	13
271	34745_at	4
272	34803_at	13
273	34898_at	4
274	34953_i_at	4
275	34954_r_at	4
276	34955_at	13
277	34973_at	4
278	34984_at	4
279	34988_at	4
280	35020_at	4
281	35021_at	4
282	35025_at	4
283	35028_at	4
284	35039_at	4
285	35053_at	4

286	35061_at	4
287	35063_at	4
288	35081_at	13
289	35105_at	13
290	35107_at	13
291	35110_at	13
292	35131_at	4
293	35134_at	4
294	35140_at	13
295	35147_at	13
296	35164_at	4
297	35181_at	4
298	35182_f_at	4
299	35193_at	13
300	35213_at	13
301	35214_at	4
302	35215_at	4
303	35220_at	4
304	35285_at	4
305	35306_at	4
306	35344_at	13
307	35356_at	4
308	35357_at	4
309	35371_at	4
310	35372_r_at	4
311	35400_at	13
312	35410_at	4
313	35435_s_at	4
314	35437_at	4
315	35469_at	13
316	35470_at	13
317	35471_g_at	13
318	35481_at	13
319	35507_at	4
320	35523_at	4
321	35554_f_at	13
322	35555_r_at	13
323	35591_at	4
324	35656_at	13
325	35662_at	4

326	35664_at	4
327	35678_at	4
328	35689_at	4
329	35698_at	4
330	35725_at	13
331	35730_at	4
332	35777_at	4
333	35793_at	4
334	35827_at	4
335	35837_at	4
336	35845_at	4
337	35871_s_at	4
338	35877_at	13
339	35904_at	13
340	35939_s_at	13
341	35940_at	13
342	35949_at	13
343	35972_at	13
344	35989_at	4
345	35991_at	4
346	36012_at	13
347	36013_at	4
348	36017_at	13
349	36021_at	4
350	36031_at	13
351	36046_at	4
352	36047_at	4
353	36065_at	4
354	36080_at	4
355	36143_at	4
356	36157_at	4
357	36188_at	13
358	36194_at	4
359	36212_at	13
360	36243_at	4
361	36247_f_at	4
362	36269_at	4
363	36274_at	13
364	36358_at	4
365	36363_at	4

366	36433_at	4
367	36434_r_at	4
368	36510_at	13
369	36521_at	13
370	36606_at	4
371	36622_at	4
372	36627_at	4
373	36659_at	13
374	36717_at	4
375	36788_at	13
376	367_at	13
377	36814_at	4
378	36830_at	13
379	36913_at	4
380	36914_at	4
381	36915_at	4
382	36918_at	4
383	36939_at	4
384	36968_s_at	13
385	36990_at	4
386	37006_at	4
387	37019_at	4
388	37023_at	13
389	37056_at	4
390	37058_at	4
391	37062_at	4
392	37067_at	13
393	37079_at	13
394	37099_at	13
395	37109_at	13
396	37154_at	13
397	37170_at	4
398	37172_at	13
399	37173_at	4
400	37187_at	4
401	37206_at	4
402	37219_at	4
403	37223_at	4
404	37243_at	4
405	37244_at	13

406	37280_at	4
407	37282_at	4
408	37291_r_at	4
409	37303_at	13
410	37322_s_at	4
411	37323_r_at	4
412	37356_r_at	4
413	37366_at	4
414	37404_at	4
415	37416_at	4
416	37472_at	4
417	37518_at	13
418	37520_at	4
419	37521_s_at	4
420	37522_r_at	4
421	37571_at	13
422	37578_at	4
423	37593_at	13
424	37619_at	4
425	37658_at	13
426	37707_i_at	4
427	37708_r_at	4
428	37723_at	4
429	37747_at	4
430	37748_at	4
431	37752_at	4
432	37757_at	13
433	37767_at	4
434	37840_at	4
435	37926_at	13
436	37930_at	13
437	37964_at	4
438	38008_at	4
439	38015_at	4
440	38016_at	4
441	38024_at	4
442	38025_r_at	4
443	38035_at	13
444	38065_at	4
445	38102_at	13

446	38120_at	4
447	38168_at	4
448	38254_at	4
449	38304_r_at	13
450	38353_at	13
451	38375_at	13
452	38438_at	4
453	38485_at	4
454	38488_s_at	4
455	38489_at	4
456	38587_at	4
457	38606_at	4
458	38615_at	13
459	38639_at	4
460	38643_at	4
461	38649_at	13
462	38714_at	4
463	38715_at	4
464	38736_at	4
465	38751_i_at	4
466	38752_r_at	4
467	38767_at	4
468	38768_at	4
469	38778_at	4
470	38821_at	4
471	38825_at	4
472	38838_at	4
473	38854_at	4
474	38891_at	4
475	38923_at	4
476	38957_at	13
477	38972_at	13
478	38988_at	4
479	39028_at	13
480	39032_at	13
481	39037_at	4
482	39056_at	4
483	39083_at	4
484	39131_at	13
485	39132_at	4

486	39208_i_at	4
487	39209_r_at	4
488	39224_at	4
489	39256_at	13
490	39257_at	13
491	39269_at	13
492	39295_s_at	4
493	39297_at	13
494	39333_at	13
495	39337_at	4
496	39355_at	4
497	39369_at	4
498	39380_at	4
499	39382_at	4
500	39405_at	13
501	39469_s_at	13
502	39475_at	4
503	39481_at	4
504	39488_at	13
505	39489_g_at	13
506	39535_at	4
507	39536_at	4
508	39554_at	4
509	39555_at	4
510	39576_at	4
511	39579_at	13
512	39600_at	4
513	39634_at	4
514	39662_s_at	4
515	39665_at	4
516	39680_at	4
517	39690_at	4
518	39698_at	4
519	39734_at	4
520	39746_at	4
521	39748_at	13
522	39758_f_at	13
523	39777_at	13
524	39786_at	4
525	39847_at	4

526	39850_at	4
527	39851_at	4
528	39852_at	13
529	39878_at	13
530	39897_at	4
531	39924_at	13
532	39929_at	4
533	39955_at	13
534	39960_at	4
535	39979_at	13
536	40018_at	13
537	40058_s_at	4
538	40059_r_at	4
539	40060_r_at	4
540	40067_at	13
541	40072_at	13
542	40082_at	4
543	400_at	13
544	40114_at	4
545	40121_at	4
546	40148_at	4
547	40180_at	13
548	40181_f_at	13
549	40199_at	4
550	40217_s_at	4
551	40218_at	4
552	40225_at	4
553	40226_at	4
554	40272_at	4
555	40310_at	4
556	40312_at	13
557	40323_at	4
558	40349_at	4
559	40354_at	4
560	40392_at	13
561	40404_s_at	13
562	40449_at	4
563	40454_at	4
564	40456_at	4
565	40473_at	13

566	40492_at	4
567	40530_at	4
568	40570_at	13
569	40576_f_at	4
570	40633_at	13
571	40681_at	13
572	40697_at	4
573	40710_at	4
574	40711_at	4
575	40727_at	4
576	40746_at	4
577	40770_f_at	4
578	40772_at	4
579	40773_at	4
580	40818_at	4
581	40828_at	13
582	40839_at	13
583	40853_at	4
584	40880_r_at	4
585	40893_at	13
586	408_at	4
587	40908_r_at	13
588	40943_at	4
589	40970_at	13
590	40989_at	4
591	40990_at	4
592	40991_at	4
593	40992_s_at	4
594	40993_r_at	4
595	41014_s_at	4
596	41024_f_at	4
597	41025_r_at	4
598	41026_f_at	4
599	41069_at	13
600	41071_at	4
601	41104_at	4
602	41118_at	13
603	41119_f_at	13
604	41145_at	4
605	41148_at	4

606	41182_at	13
607	41191_at	4
608	41276_at	13
609	41277_at	13
610	41300_s_at	13
611	41301_at	13
612	41308_at	4
613	41309_g_at	4
614	41317_at	13
615	41318_g_at	13
616	41319_at	13
617	41376_i_at	4
618	41377_f_at	4
619	41391_at	4
620	41392_at	4
621	41402_at	4
622	41434_at	4
623	41436_at	13
624	41456_at	4
625	41459_at	13
626	41470_at	4
627	41491_s_at	13
628	41492_r_at	13
629	41493_at	13
630	41534_at	4
631	41555_at	4
632	41556_s_at	4
633	41585_at	4
634	41667_s_at	13
635	41668_r_at	13
636	41697_at	4
637	41801_at	4
638	41806_at	4
639	41860_at	13
640	431_at	4
641	504_at	4
642	507_s_at	4
643	579_at	4
644	618_at	4
645	630_at	4

646	631_g_at	4
647	655_at	4
648	690_s_at	4
649	692_s_at	4
650	764_s_at	4
651	820_at	4
652	886_at	4
653	931_at	13
654	936_s_at	4
655	948_s_at	4
656	963_at	13
657	975_at	4
658	990_at	13
659	991_g_at	13

To get this in the classic named-list format:

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

```
[1] "4" "13"
```

```
R> 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:

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

```
$`12`
```

```
[1] "1018_at" "1019_g_at" "101_at" "1021_at"
```

```
$`6`
```

```
[1] "1007_s_at" "1026_s_at" "1027_at"
```

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

```
R> 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...

```
R> 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"?

```
R> x <- hgu95av2MAP
R> pbids <- c("38912_at", "41654_at", "907_at", "2053_at", "2054_g_at",
             "40781_at")
R> x <- subset(x, Lkeys=pbids, Rkeys="18q11.2")
R> 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:

```
R> pb2cyto <- as.character(x)
R> 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:

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

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 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.

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

```
[1] 11774      2
```

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

```
[1] 12821      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.

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

```
[1] 1047      2
```

```

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

[1] 11774      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.

```

R> ## Test the multiOnly mapping
R> hasMultiProbes(multiOnly)

[1] TRUE

```

```

R> hasSingleProbes(multiOnly)

[1] FALSE

```

```

R> ## Test the singleOnly mapping
R> hasMultiProbes(singleOnly)

[1] FALSE

```

```

R> 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 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.

```
R> 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.

```
R> org.Hs.eg_dbconn()
```

You can use this connection object like this:

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

```
R> ## Obtain SYMBOLS with at least one GO BP
R> ## annotation with evidence IMP, IGI, IPI, or IDA.
R> system.time({
  bpids <- eapply(hgu95av2GO, function(x) {
    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, hgu95av2GO2PROBE)
  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))
})
R> length(ans)
R> 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:

```
R> 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:

```
R> hgu95av2ORGPKG
```

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

```
R> 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':

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

NULL

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.:

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

```
user system elapsed
0.244 0.008 0.251
```

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

NULL

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 2.15.3 (2013-03-01)

Platform: x86_64-unknown-linux-gnu (64-bit)

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=C                LC_NAME=C
[9] LC_ADDRESS=C             LC_TELEPHONE=C
[11] LC_MEASUREMENT=en_US.UTF-8 LC_IDENTIFICATION=C
```

attached base packages:

```
[1] stats      graphics  grDevices  utils      datasets  methods
[7] base
```

other attached packages:

```
[1] GO.db_2.8.0          hgu95av2.db_2.8.0    AnnotationForge_1.0.3
[4] org.Hs.eg.db_2.8.0  RSQLite_0.11.2       DBI_0.2-5
[7] AnnotationDbi_1.20.7 Biobase_2.18.0       BiocGenerics_0.4.0
```

loaded via a namespace (and not attached):

```
[1] IRanges_1.16.6  parallel_2.15.3  stats4_2.15.3  tools_2.15.3
```