

# 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"     "hgu95av20MIM"
[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 33154 mapped keys (of 99696 keys)"
[8] "hgu95av2CHR has 11559 mapped keys (of 12625 keys)"
[9] "hgu95av2CHRLNGTHS has 93 mapped keys (of 93 keys)"
[10] "hgu95av2CHRLLOC has 11493 mapped keys (of 12625 keys)"
[11] "hgu95av2CHRLLOCEND has 11493 mapped keys (of 12625 keys)"
[12] "hgu95av2ENSEMBL has 11455 mapped keys (of 12625 keys)"
[13] "hgu95av2ENSEMBL2PROBE has 9700 mapped keys (of 27388 keys)"
[14] "hgu95av2ENTREZID has 11562 mapped keys (of 12625 keys)"
[15] "hgu95av2ENZYME has 2121 mapped keys (of 12625 keys)"
[16] "hgu95av2ENZYME2PROBE has 786 mapped keys (of 975 keys)"
[17] "hgu95av2GENENAME has 11562 mapped keys (of 12625 keys)"
[18] "hgu95av2GO has 11241 mapped keys (of 12625 keys)"
[19] "hgu95av2GO2ALLPROBES has 16108 mapped keys (of 17608 keys)"
[20] "hgu95av2GO2PROBE has 12085 mapped keys (of 13737 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] "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:

```
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] "36132_at" "35870_at"
```

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

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

```
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	38187_at	00232
2	38187_at	00983
3	38187_at	01100
4	38912_at	00232
5	38912_at	00983
6	38912_at	01100

```
R> toTable(revx)[1:6, ]
```

	probe_id	path_id
1	38187_at	00232

```

2 38187_at 00983
3 38187_at 01100
4 38912_at 00232
5 38912_at 00983
6 38912_at 01100

```

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 PF07714
4 1001_at IPI00019530 PF00041
5 1001_at IPI00019530 PF12661
6 1001_at IPI00936406 PF00041

```

```
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"  "1008_f_at" "1009_at"
```

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

```
[1] 9
```

```
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"  "1008_f_at" "1009_at"
```

```
R> 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`.

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

```
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	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	31686_at	4
103	31706_at	4
104	31744_at	4
105	31753_at	13
106	31790_at	13
107	31792_at	4
108	31805_at	4
109	31811_r_at	4
110	31847_at	13
111	31849_at	13
112	31851_at	13
113	31876_r_at	4
114	31894_at	4
115	31969_i_at	4
116	31970_r_at	4
117	32006_r_at	4
118	32026_s_at	4
119	32080_at	4
120	32102_at	13
121	32145_at	4
122	32146_s_at	4
123	32147_at	13
124	32148_at	13
125	32163_f_at	4

126	32180_s_at	4
127	32220_at	13
128	32299_at	4
129	32349_at	4
130	32353_at	4
131	32357_at	4
132	32368_at	13
133	32393_s_at	4
134	32439_at	13
135	32446_at	4
136	32449_at	4
137	32465_at	4
138	32482_at	13
139	32506_at	4
140	32507_at	4
141	32570_at	4
142	32580_at	4
143	32595_at	4
144	32602_at	4
145	32641_at	13
146	32675_at	4
147	32703_at	4
148	32768_at	13
149	32769_at	4
150	32770_at	4
151	32771_at	4
152	32812_at	4
153	32822_at	4
154	32832_at	4
155	32862_at	13
156	32906_at	13
157	32979_at	4
158	32986_s_at	13
159	32998_at	4
160	33013_at	4
161	33050_at	4
162	33068_f_at	4
163	33069_f_at	4
164	33100_at	4
165	33150_at	4

166	33151_s_at	4
167	33155_at	4
168	33156_at	4
169	33168_at	13
170	33171_s_at	4
171	33172_at	4
172	33173_g_at	4
173	33199_at	13
174	33208_at	13
175	33241_at	4
176	33249_at	4
177	33267_at	4
178	33276_at	13
179	33299_at	4
180	33318_at	13
181	33356_at	4
182	33359_at	4
183	33369_at	4
184	33370_r_at	4
185	33382_at	4
186	33483_at	4
187	33488_at	4
188	33490_at	4
189	33494_at	4
190	33519_at	4
191	33520_at	13
192	33525_at	4
193	33526_at	4
194	33529_at	4
195	33536_at	4
196	33544_at	4
197	33564_at	4
198	33576_at	13
199	33584_at	4
200	33596_at	4
201	33657_at	4
202	33672_f_at	4
203	33673_r_at	4
204	33687_at	13
205	33700_at	13

206	33733_at	4
207	33791_at	13
208	33823_at	4
209	33827_at	13
210	33837_at	4
211	33859_at	13
212	33975_at	4
213	33990_at	4
214	33991_g_at	4
215	33992_at	4
216	33997_at	4
217	34021_at	4
218	34022_at	4
219	34026_at	13
220	34029_at	4
221	34048_at	4
222	34051_at	13
223	34058_at	4
224	34075_at	4
225	34122_at	4
226	34131_at	4
227	34144_at	4
228	34145_at	4
229	34149_at	4
230	34170_s_at	4
231	34181_at	4
232	34198_at	4
233	34211_at	13
234	34239_at	13
235	34240_s_at	13
236	34247_at	4
237	34248_at	4
238	34275_s_at	4
239	34284_at	13
240	34307_at	13
241	34319_at	4
242	34324_at	13
243	34334_at	13
244	34335_at	13
245	34341_at	4

246	34342_s_at	4
247	34353_at	4
248	34398_at	13
249	34411_at	4
250	34423_at	4
251	34459_at	13
252	34476_r_at	4
253	34482_at	4
254	34512_at	4
255	34551_at	4
256	34564_at	4
257	34565_at	4
258	34578_at	13
259	34583_at	13
260	34596_at	4
261	34637_f_at	4
262	34638_r_at	4
263	34657_at	13
264	34672_at	13
265	34745_at	4
266	34803_at	13
267	34953_i_at	4
268	34954_r_at	4
269	34955_at	13
270	34973_at	4
271	34984_at	4
272	34988_at	4
273	35020_at	4
274	35021_at	4
275	35025_at	4
276	35028_at	4
277	35039_at	4
278	35053_at	4
279	35061_at	4
280	35063_at	4
281	35081_at	13
282	35105_at	13
283	35107_at	13
284	35110_at	13
285	35131_at	4

286	35134_at	4
287	35140_at	13
288	35147_at	13
289	35164_at	4
290	35181_at	4
291	35182_f_at	4
292	35193_at	13
293	35213_at	13
294	35214_at	4
295	35215_at	4
296	35220_at	4
297	35285_at	4
298	35306_at	4
299	35344_at	13
300	35356_at	4
301	35357_at	4
302	35371_at	4
303	35372_r_at	4
304	35400_at	13
305	35410_at	4
306	35435_s_at	4
307	35437_at	4
308	35469_at	13
309	35470_at	13
310	35471_g_at	13
311	35481_at	13
312	35507_at	4
313	35523_at	4
314	35554_f_at	13
315	35555_r_at	13
316	35591_at	4
317	35656_at	13
318	35662_at	4
319	35664_at	4
320	35678_at	4
321	35689_at	4
322	35698_at	4
323	35725_at	13
324	35730_at	4
325	35777_at	4

326	35793_at	4
327	35827_at	4
328	35837_at	4
329	35845_at	4
330	35871_s_at	4
331	35877_at	13
332	35904_at	13
333	35939_s_at	13
334	35940_at	13
335	35949_at	13
336	35972_at	13
337	35989_at	4
338	35991_at	4
339	36012_at	13
340	36013_at	4
341	36017_at	13
342	36021_at	4
343	36031_at	13
344	36046_at	4
345	36047_at	4
346	36065_at	4
347	36080_at	4
348	36143_at	4
349	36157_at	4
350	36188_at	13
351	36194_at	4
352	36212_at	13
353	36243_at	4
354	36247_f_at	4
355	36269_at	4
356	36274_at	13
357	36358_at	4
358	36363_at	4
359	36433_at	4
360	36434_r_at	4
361	36510_at	13
362	36521_at	13
363	36606_at	4
364	36622_at	4
365	36627_at	4

366	36659_at	13
367	36717_at	4
368	36788_at	13
369	367_at	13
370	36814_at	4
371	36830_at	13
372	36913_at	4
373	36914_at	4
374	36915_at	4
375	36918_at	4
376	36939_at	4
377	36968_s_at	13
378	36990_at	4
379	37006_at	4
380	37019_at	4
381	37023_at	13
382	37056_at	4
383	37058_at	4
384	37062_at	4
385	37067_at	13
386	37079_at	13
387	37099_at	13
388	37109_at	13
389	37154_at	13
390	37170_at	4
391	37172_at	13
392	37173_at	4
393	37187_at	4
394	37206_at	4
395	37219_at	4
396	37223_at	4
397	37243_at	4
398	37244_at	13
399	37280_at	4
400	37282_at	4
401	37291_r_at	4
402	37303_at	13
403	37322_s_at	4
404	37323_r_at	4
405	37356_r_at	4

406	37366_at	4
407	37404_at	4
408	37416_at	4
409	37472_at	4
410	37518_at	13
411	37520_at	4
412	37521_s_at	4
413	37522_r_at	4
414	37571_at	13
415	37578_at	4
416	37593_at	13
417	37619_at	4
418	37658_at	13
419	37707_i_at	4
420	37708_r_at	4
421	37723_at	4
422	37747_at	4
423	37748_at	4
424	37752_at	4
425	37757_at	13
426	37758_s_at	13
427	37767_at	4
428	37840_at	4
429	37926_at	13
430	37930_at	13
431	37964_at	4
432	38008_at	4
433	38016_at	4
434	38024_at	4
435	38025_r_at	4
436	38035_at	13
437	38065_at	4
438	38102_at	13
439	38120_at	4
440	38168_at	4
441	38254_at	4
442	38304_r_at	13
443	38353_at	13
444	38375_at	13
445	38438_at	4

446	38485_at	4
447	38488_s_at	4
448	38489_at	4
449	38587_at	4
450	38606_at	4
451	38615_at	13
452	38643_at	4
453	38649_at	13
454	38714_at	4
455	38715_at	4
456	38736_at	4
457	38751_i_at	4
458	38752_r_at	4
459	38767_at	4
460	38768_at	4
461	38778_at	4
462	38821_at	4
463	38825_at	4
464	38838_at	4
465	38854_at	4
466	38891_at	4
467	38957_at	13
468	38972_at	13
469	38988_at	4
470	39028_at	13
471	39032_at	13
472	39037_at	4
473	39056_at	4
474	39083_at	4
475	39131_at	13
476	39132_at	4
477	39208_i_at	4
478	39209_r_at	4
479	39224_at	4
480	39256_at	13
481	39257_at	13
482	39269_at	13
483	39295_s_at	4
484	39297_at	13
485	39333_at	13

486	39337_at	4
487	39355_at	4
488	39369_at	4
489	39380_at	4
490	39382_at	4
491	39405_at	13
492	39469_s_at	13
493	39475_at	4
494	39481_at	4
495	39488_at	13
496	39489_g_at	13
497	39535_at	4
498	39536_at	4
499	39554_at	4
500	39555_at	4
501	39576_at	4
502	39579_at	13
503	39600_at	4
504	39634_at	4
505	39662_s_at	4
506	39665_at	4
507	39680_at	4
508	39690_at	4
509	39698_at	4
510	39734_at	4
511	39746_at	4
512	39748_at	13
513	39758_f_at	13
514	39777_at	13
515	39786_at	4
516	39847_at	4
517	39850_at	4
518	39851_at	4
519	39852_at	13
520	39878_at	13
521	39897_at	4
522	39924_at	13
523	39929_at	4
524	39955_at	13
525	39960_at	4

526	39979_at	13
527	40018_at	13
528	40058_s_at	4
529	40059_r_at	4
530	40060_r_at	4
531	40067_at	13
532	40072_at	13
533	40082_at	4
534	400_at	13
535	40114_at	4
536	40121_at	4
537	40148_at	4
538	40180_at	13
539	40181_f_at	13
540	40199_at	4
541	40217_s_at	4
542	40218_at	4
543	40225_at	4
544	40226_at	4
545	40272_at	4
546	40310_at	4
547	40312_at	13
548	40323_at	4
549	40349_at	4
550	40354_at	4
551	40392_at	13
552	40404_s_at	13
553	40449_at	4
554	40454_at	4
555	40456_at	4
556	40473_at	13
557	40492_at	4
558	40530_at	4
559	40570_at	13
560	40576_f_at	4
561	40633_at	13
562	40681_at	13
563	40697_at	4
564	40710_at	4
565	40711_at	4

566	40727_at	4
567	40746_at	4
568	40770_f_at	4
569	40772_at	4
570	40773_at	4
571	40818_at	4
572	40828_at	13
573	40839_at	13
574	40853_at	4
575	40880_r_at	4
576	40893_at	13
577	408_at	4
578	40908_r_at	13
579	40943_at	4
580	40970_at	13
581	40989_at	4
582	40990_at	4
583	40991_at	4
584	40992_s_at	4
585	40993_r_at	4
586	41014_s_at	4
587	41024_f_at	4
588	41025_r_at	4
589	41026_f_at	4
590	41069_at	13
591	41071_at	4
592	41104_at	4
593	41118_at	13
594	41119_f_at	13
595	41145_at	4
596	41148_at	4
597	41182_at	13
598	41191_at	4
599	41276_at	13
600	41277_at	13
601	41300_s_at	13
602	41301_at	13
603	41308_at	4
604	41309_g_at	4
605	41317_at	13

606	41318_g_at	13
607	41319_at	13
608	41376_i_at	4
609	41377_f_at	4
610	41391_at	4
611	41392_at	4
612	41402_at	4
613	41434_at	4
614	41436_at	13
615	41456_at	4
616	41459_at	13
617	41470_at	4
618	41491_s_at	13
619	41492_r_at	13
620	41493_at	13
621	41534_at	4
622	41555_at	4
623	41556_s_at	4
624	41585_at	4
625	41667_s_at	13
626	41668_r_at	13
627	41697_at	4
628	41801_at	4
629	41806_at	4
630	41860_at	13
631	431_at	4
632	504_at	4
633	507_s_at	4
634	579_at	4
635	618_at	4
636	630_at	4
637	631_g_at	4
638	655_at	4
639	690_s_at	4
640	692_s_at	4
641	764_s_at	4
642	820_at	4
643	886_at	4
644	931_at	13
645	936_s_at	4

```

646  948_s_at      4
647   963_at     13
648   975_at      4
649   990_at     13
650  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] "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" "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...

```

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" "1026_s_at"  "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] 11562    2
```

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

```
[1] 13342    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] 1780    2
```

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

```
[1] 11562    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({
  bpidids <- 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, hgu95av2G02PROBE)
wantedp <- lapply(g2p, function(x) {
    x[names(x) %in% c("IMP", "IGI", "IPI", "IDA")]
})
wantedp <- wantedp[sapply(wantedp, length) > 0]
wantedp <- unique(unlist(wantedp))
ans <- unlist(mget(wantedp, hgu95av2SYMBOL))
})
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.gene_info AS zz
  zz <- dbGetQuery(hgu95av2_dbconn(), SQL)
})
```

```
      user  system elapsed
0.180    0.012    0.273
```

```
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 3.0.2 (2013-09-25)

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

other attached packages:

```
[1] GO.db_2.10.1 hgu95av2.db_2.10.1 AnnotationForge_1.4.0
[4] org.Hs.eg.db_2.10.1 RSQLite_0.11.4 DBI_0.2-7
[7] AnnotationDbi_1.24.0 Biobase_2.22.0 BiocGenerics_0.8.0
```

loaded via a namespace (and not attached):

```
[1] IRanges_1.20.0 stats4_3.0.2 tools_3.0.2
```