Marc Carlson, Herve Pages, Seth Falcon, Nianhua Li

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NOTE The 'bimap' interface to annotation resources is not recommend; instead, use the approach in the vignette Introduction To Bioconductor Annotation Packages.

1 Introduction

1.0.1 Purpose

AnnotationDbi is used primarily to create mapping objects that allow easy access from R to underlying annotation databases. As such, it acts as the R interface for all the standard annotation packages. Underlying each AnnotationDbi supported annotation package is at least one (and often two) annotation databases. AnnotationDbi also provides schemas for theses databases. For each supported model organism, a standard gene centric database is maintained from public sources and is packaged up as an appropriate organism or "org" package.

1.0.2 Database Schemas

For developers, a lot of the benefits of having the information loaded into a real database will require some knowledge about the database schema. For this reason the schemas that were used in the creation of each database type are included in AnnotationDbi. The currently supported schemas are listed in the DBschemas directory of AnnotationDbi. But it is also possible to simply print out the schema that a package is currently using by using its "_dbschema" method.

There is one schema/database in each kind of package. These schemas specify which tables and indices will be present for each package of that type. The schema that a particular package is using is also listed when you type the name of the package as a function to obtain quality control information.

The code to make most kinds of the new database packages is also included in AnnotationDbi. Please see the vignette on SQLForge for more details on how to make additional database packages.

1.0.3 Internal schema Design of org packages

The current design of the organism packages is deliberately simple and gene centric. Each table in the database contains a unique kind of information and also an internal identifier called _id. The internal _id has no meaning outside of the context of a single database. But _id does connect all the data within a single database.

As an example if we wanted to connect the values in the genes table with the values in the kegg table, we could simply join the two tables using the internal _id column. It is very important to note however that _id does not have any absolute significance. That is, it has no meaning outside of the context of the database where it is used. It is tempting to think that an _id could have such significance because within a single database, it looks and behaves similarly to an entrez gene ID. But _id is definitely NOT an entrez gene ID. The entrez gene IDs are in another table entirely, and can be connected to using the internal _id just like all the other meaningful information inside these databases. Each organism package is centered around one type of gene identifier. This identifier is found as the gene_id field in the genes table and is both the central ID for the database as well as the foreign key that chip packages should join to.

The chip packages are 'lightweight', and only contain information about the basic probe to gene mapping. You might wonder how such packages can provide access to all the other information that they do. This is possible because all the other data provided by chip packages comes from joins that are performed by AnnotationDbi behind the scenes at run time. All chip packages have a dependency on at least one organism package. The name of the organism package being depended on can be found by looking at its "ORGPKG" value. To learn about the schema from the appropriate organism package, you will need to look at the "_dbschema" method for that package. In the case of the chip packages, the gene_id that in these packages is mapped to the probe_ids, is used as a foreign key to the appropriate organism package.

Specialized packages like the packages for GO and KEGG, will have their own schemas but will also adhere to the use of an internal _id for joins between their tables. As with the organism packages, this _id is not suitable for use as a foreign key.

For a complete listing of the different schemas used by various packages, users can use the available.dbschemas function. This list will also tell you which model organisms are supported.

```
library(DBI)
library(org.Hs.eg.db)

## Loading required package: AnnotationDbi

## Loading required package: stats4

## Loading required package: BiocGenerics

## Loading required package: parallel
```

```
##
## Attaching package: 'BiocGenerics'
## The following objects are masked from 'package:parallel':
##
      clusterApply, clusterApplyLB, clusterCall, clusterEvalQ,
##
      clusterExport, clusterMap, parApply, parCapply, parLapply,
##
      parLapplyLB, parRapply, parSapply, parSapplyLB
## The following objects are masked from 'package:stats':
##
      IQR, mad, sd, var, xtabs
##
## The following objects are masked from 'package:base':
##
      Filter, Find, Map, Position, Reduce, anyDuplicated, append,
##
      as.data.frame, cbind, colMeans, colSums, 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, rowMeans, rowSums,
##
##
      rownames, sapply, setdiff, sort, table, tapply, union, unique,
      unsplit, which, which.max, which.min
##
## Loading required package: Biobase
## Welcome to Bioconductor
##
      Vignettes contain introductory material; view with
##
      'browseVignettes()'. To cite Bioconductor, see
##
      'citation("Biobase")', and for packages 'citation("pkgname")'.
## Loading required package: IRanges
## Loading required package: S4Vectors
##
## Attaching package: 'S4Vectors'
## The following object is masked from 'package:base':
##
##
      expand.grid
##
library(AnnotationForge)
available.dbschemas()
```

2 Examples

2.0.1 Basic information

The AnnotationDbi package provides an interface to SQLite-based annotation packages. Each SQLite-based annotation package (identified by a ".db" suffix in the package name) contains a number of AnnDbBimap objects in place of the environment objects found in the old-style environment-based annotation packages. The API provided by AnnotationDbi allows you to treat the AnnDbBimap objects like environment instances. For example, the functions [[, get, mget, and ls all behave the same as they did with the older environment based annotation packages. In addition, new methods like [, toTable, subset and others provide some additional flexibility in accessing the annotation data.

```
library(hgu95av2.db)
##
```

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

```
ls("package:hgu95av2.db")
    [1] "hgu95av2"
                                 "hqu95av2.db"
    [3] "hgu95av2ACCNUM"
                                 "hgu95av2ALIAS2PR0BE"
                                 "hqu95av2CHRLENGTHS"
    [5] "hgu95av2CHR"
   [7] "hgu95av2CHRL0C"
                                 "hgu95av2CHRL0CEND"
##
   [9] "hgu95av2ENSEMBL"
                                 "hgu95av2ENSEMBL2PR0BE"
## [11] "hgu95av2ENTREZID"
                                 "hqu95av2ENZYME"
## [13] "hqu95av2ENZYME2PR0BE"
                                 "hgu95av2GENENAME"
## [15] "hgu95av2G0"
                                 "hgu95av2G02ALLPR0BES"
## [17] "hgu95av2G02PR0BE"
                                 "hgu95av2MAP"
## [19] "hqu95av2MAPCOUNTS"
                                 "hgu95av20MIM"
## [21] "hgu95av20RGANISM"
                                 "hgu95av20RGPKG"
## [23] "hgu95av2PATH"
                                 "hgu95av2PATH2PR0BE"
## [25] "hgu95av2PFAM"
                                 "hgu95av2PMID"
## [27] "hqu95av2PMID2PR0BE"
                                 "hgu95av2PR0SITE"
## [29] "hgu95av2REFSEQ"
                                 "hgu95av2SYMB0L"
## [31] "hgu95av2UNIGENE"
                                 "hgu95av2UNIPROT"
## [33] "hgu95av2_dbInfo"
                                 "hgu95av2_dbconn"
## [35] "hgu95av2_dbfile"
                                 "hgu95av2_dbschema"
```

Exercise 1

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

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

```
qcdata = capture.output(hgu95av2())
head(qcdata, 20)
   [1] "Quality control information for hqu95av2:"
##
   [2] ""
   [3] ""
##
   [4] "This package has the following mappings:"
   [5] ""
##
   [6] "hgu95av2ACCNUM has 12625 mapped keys (of 12625 keys)"
   [7] "hgu95av2ALIAS2PR0BE has 34238 mapped keys (of 120180 keys)"
## [8] "hgu95av2CHR has 11472 mapped keys (of 12625 keys)"
## [9] "hgu95av2CHRLENGTHS has 93 mapped keys (of 455 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] "hgu95av2ENSEMBL2PR0BE has 9545 mapped keys (of 28931 keys)"
## [14] "hgu95av2ENTREZID has 11474 mapped keys (of 12625 keys)"
## [15] "hqu95av2ENZYME has 2097 mapped keys (of 12625 keys)"
## [16] "hqu95av2ENZYME2PR0BE 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] "hgu95av2G02ALLPR0BES has 18521 mapped keys (of 21861 keys)"
## [20] "hgu95av2G02PR0BE has 13971 mapped keys (of 17120 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(0xalbeef)
probes <- sample(all_probes, 5)
probes

## [1] "31882_at" "38780_at" "37033_s_at" "1702_at" "31610_at"</pre>
```

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))</pre>
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.

?hgu95av2CHRL0C

Exercise 2

For the probes in 'probes' above, use the annotation mappings to find the chromosome start locations.

2.0.2 Manipulating Bimap Objects

Many filtering operations on the annotation *Bimap* objects require conversion of the *AnnDbBimap* into a *list*. In general, converting to lists will not be the most efficient way to filter the annotation data when using a SQLite-based package. Compare the following two examples for how you could get the 1st ten elements of the hgu95av2SYMBOL mapping. In the 1st case we have to get the entire mapping into list form, but in the second case we first subset the mapping object itself and this allows us to only convert the ten elements that we care about.

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

There are many different kinds of *Bimap* objects in AnnotationDbi, but most of them are of class *AnnDbBimap*. All /RclassBimap objects represent data as a set of left and right keys. The typical usage of these mappings is to search for right keys that match a set of left keys that have been supplied by the user. But sometimes it is also convenient to go in the opposite direction.

The annotation packages provide many reverse maps as objects in the package name space for backwards compatibility, but the reverse mappings of almost any map is also available using revmap. Since the data are stored as tables, no extra disk space is needed to provide reverse mappings.

```
unlist(mget(syms, revmap(hgu95av2SYMB0L)))
## 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] "36132_at" "35870_at"
```

Note that in the case of the PATH map, we don't need to use revmap(x) because hgu95av2.db already provides the PATH2PROBE map:

```
x <- hgu95av2PATH
## except for the name, this is exactly revmap(x)
revx <- hgu95av2PATH2PR0BE
revx2 <- revmap(x, objName="PATH2PR0BE")
revx2

## PATH2PR0BE map for chip hgu95av2 (object of class "ProbeAnnDbBimap")
identical(revx, revx2)

## [1] TRUE
as.list(revx["00300"])

## $`00300`
## [1] "36132_at" "35870_at"</pre>
```

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

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

Exercise 3

Given the following set of RefSeq IDs: c("NG_005114","NG_007432","NG_008063"), Find the Entrez Gene IDs that would correspond to those. Then find the GO terms that are associated with those entrez gene IDs.

org. Hs. eg. db packages.

2.0.3 The Contents and Structure of Bimap Objects

Sometimes you may want to display or subset elements from an individual map. A *Bimap* interface is available to access the data in table (*data.frame*) format using [and toTable.

```
head(toTable(hgu95av2G0[probes]))
##
     probe_id
                   go_id Evidence Ontology
## 1 1702_at G0:0000165
                              TAS
                                         BP
## 2 1702_at G0:0002437
                              IEA
                                         BP
## 3 1702_at G0:0002664
                              IMP
                                         BP
## 4 1702_at G0:0006915
                              TAS
                                         BP
## 5 1702_at G0:0006924
                                         BP
                              IEA
## 6 1702_at G0:0006954
                              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 is is necessary to only display information that is directly associated with the left to right links in a *Bimap*, then the links function can be used. The links returns a data frame with one row for each link in the bimap that it is applied to. It only reports the left and right keys along with any attributes that are attached to the edge between these two values.

Note that the order of the cols returned by toTable does not depend on the direction of the map. We refer to it as an 'undirected method':

```
toTable(x)[1:6, ]
    probe_id path_id
## 1 1000_at 04010
## 2 1000_at 04012
## 3 1000_at 04062
## 4 1000_at 04114
## 5 1000_at 04150
## 6 1000_at 04270
toTable(revx)[1:6, ]
    probe_id path_id
## 1 1000_at
              04010
## 2 1000_at
              04012
## 3 1000_at 04062
## 4 1000_at 04114
## 5 1000_at 04150
## 6 1000_at
              04270
```

Notice however that the Lkeys are always on the left (1st col), the Rkeys always in the 2nd col

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

```
length(x)

## [1] 12625

length(revx)

## [1] 229

allProbeSetIds <- keys(x)
allKEGGIds <- keys(revx)</pre>
```

There are more 'undirected' methods listed below:

Notice how they give the same result for x and revmap(x)

You might be tempted to think that Lkeys and Llength will tell you all that you want to know about the left keys. But things are more complex than this, because not all keys are mapped. Often, you will only want to know about the keys that are mapped (ie. the ones that have a corresponding Rkey). To learn this you want to use the mappedkeys or the undirected variants mappedLkeys and mappedRkeys. Similarily, the count.mappedkeys, count.mappedLkeys and count.mappedRkeys methods are very fast ways to determine how many keys are mapped. Accessing keys like this is usually very fast and so it can be a decent strategy to subset the mapping by 1st using the mapped keys that you want to find.

```
x = hgu95av2ENTREZID[1:10]
## Directed methods
                        # mapped keys
mappedkeys(x)
## [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
                               "1002_f_at" "1003_s_at" "1004_at"
## [1] "1000_at"
                   "1001_at"
## [6] "1005_at"
                               "1008_f_at" "1009_at"
                   "1006_at"
count.mappedLkeys(x)
                        # nb of mapped Lkeys
## [1] 9
```

If you want to find keys that are not mapped to anything, you might want to use isNA.

```
y = hgu95av2ENTREZID[isNA(hgu95av2ENTREZID)]  # usage like is.na()
Lkeys(y)[1:4]
## [1] "1007_s_at" "1047_s_at" "1089_i_at" "108_g_at"
```

Exercise 4

How many probesets do not have a GO mapping for the hgu95av2.db package? How many have no mapping? Find a probeset that has a GO mapping. Now look at the GO mappings for this probeset in table form.

2.0.4 Some specific examples

Lets use what we have learned to get information about the probes that are are not assigned to a chromosome:

```
x <- hgu95av2CHR
Rkeys(x)
## [1] "19" "12" "8" "14" "3" "2" "17" "16" "9" "X" "6" "1" "7"
## [14] "10" "11" "22" "5" "18" "15" "Y" "20" "21" "4" "13" "MT" "Un"
chroms \leftarrow Rkeys(x)[23:24]
chroms
## [1] "4" "13"
Rkeys(x) <- chroms</pre>
toTable(x)
##
       probe_id chromosome
## 1 1029_s_at
## 2
       1036_at
                       4
## 3
       1058_at
                      13
## 4
        1065_at
                       13
## 5
       1115_at
                      4
       1189_at
## 6
                       13
## 7
       1198_at
                       13
## 8
       1219_at
## 9 1220_g_at
                       4
## 10
       1249_at
## 11
        1285_at
                       4
## 12
       1303_at
                       4
## 13
       1325_at
                       4
## 14
      1348_s_at
                       13
## 15
      1369_s_at
## 16
       1377_at
                       4
## 17
      1378_g_at
                       4
## 18
      1451_s_at
                       13
## 19
       1503_at
                       13
      1507_s_at
## 20
                       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
                         4
         1593_at
## 34
        1597_at
                        13
## 35
       1598_g_at
                        13
## 36
         159_at
                        4
## 37
         1600_at
                        4
## 38
                        4
        1604_at
## 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
       1883_s_at
                         4
## 56
## 57
       1888_s_at
                        4
## 58
       1900_at
                        13
## 59
       1905_s_at
                        13
## 60
        1913_at
                        4
## 61
        1914_at
                        13
                        13
## 62
        1931_at
## 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
                      4
## 83
      31333_at
## 84
                       4
      31345_at
## 85
      31349_at
                       4
## 86
      31356_at
## 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
                      4
## 100 31670_s_at
## 101 31684_at
                       4
## 102 31706_at
## 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
## 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
## 139 32507_at
                      4
## 140 32570_at
## 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
                     4
      32998_at
## 159
      33013_at
                     4
## 160 33068_f_at
                      4
## 161 33069_f_at
## 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
## 169 33172_at
                      4
## 170 33173_g_at
                      4
## 171 33199_at
                      13
## 172 33208_at
                      13
## 173 33241_at
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## 174 33249_at
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## 175 33267_at
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## 176 33276_at
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## 177 33299_at
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## 178 33318_at
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## 179 33356_at
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## 180 33359_at
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## 181 33369_at
## 182 33370_r_at
                     4
## 183 33382_at
## 184 33483_at
                      4
## 185 33488_at
## 186 33490_at
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## 187 33494_at
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## 188 33519_at
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## 189 33520_at
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## 190 33525_at
## 191 33526_at
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## 192 33529_at
## 193 33536_at
                     4
## 194 33544_at
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## 195 33564_at
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## 196 33576_at
                    13
## 197 33584_at
## 198 33596_at
                      4
## 199 33657_at
## 200 33672_f_at
                      4
## 201 33673_r_at
                      4
## 202 33687_at
                      13
## 203 33700_at
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## 204 33733_at
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## 205 33791_at
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## 206 33823_at
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## 207 33827_at
                      13
## 208 33837_at
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## 209 33859_at
                      13
## 210 33975_at
                      4
## 211 33990_at
                       4
## 212 33991_g_at
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```

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## 213
       33992_at
## 214 33997_at
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## 215 34021_at
                       4
## 216 34022_at
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## 217 34026_at
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## 218 34029_at
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## 219 34048_at
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## 220 34051_at
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## 221 34058_at
## 222 34075_at
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## 223 34122_at
                       4
## 224 34131_at
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## 225 34144_at
                       4
## 226 34145_at
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## 227 34149_at
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## 228 34170_s_at
## 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
## 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
## 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
## 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
## 267 34954_r_at
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## 268 34955_at
                    13
## 269 34973_at
                     4
## 270 34984_at
                      4
## 271 34988_at
## 272 35020_at
                      4
## 273 35021_at
## 274 35025_at
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## 275 35028_at
## 276 35039_at
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## 277 35053_at
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## 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
## 290 35182_f_at
                      4
## 291 35193_at
                      13
## 292 35213_at
                      13
## 293 35214_at
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## 294 35215_at
                     4
## 295 35220_at
                      4
## 296 35285_at
## 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
```

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## 303
       35400_at
                       13
## 304 35410_at
                      4
## 305 35435_s_at
                       4
## 306 35437_at
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## 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
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## 315
      35564_at
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## 316 35591_at
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## 317 35656_at
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## 318 35662_at
## 319 35664_at
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## 320 35678_at
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## 321 35698_at
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## 322 35725_at
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## 323 35730_at
                       4
## 324 35777_at
                       4
## 325 35793_at
                      4
## 326 35827_at
                       4
## 327 35837_at
## 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
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## 339 36013_at
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## 340 36017_at
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## 341 36021_at
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## 342 36031_at
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## 343 36046_at
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## 344 36047_at
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## 345
       36065_at
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## 346 36080_at
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## 347
       36143_at
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## 348
       36157_at
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## 349 36188_at
                      13
## 350 36194_at
                       4
## 351 36212_at
                      13
## 352 36243_at
                      4
## 353 36247_f_at
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## 354 36269_at
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## 355 36274_at
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## 356 36358_at
## 357 36363_at
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## 358 36433_at
                       4
## 359 36434_r_at
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## 360
      36510_at
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## 361 36521_at
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## 362 36606_at
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## 363 36622_at
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## 364 36627_at
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## 365 36659_at
                      13
## 366 36717_at
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## 367 36788_at
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## 368 367_at
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## 369 36814_at
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## 370 36830_at
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## 371 36913_at
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## 372 36914_at
## 373 36915_at
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## 374 36918_at
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## 375
       36939_at
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## 376 36968_s_at
                      13
                     4
## 377
       36990_at
## 378
      37006_at
                       4
## 379 37019_at
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## 380 37023_at
                      13
## 381 37056_at
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## 382 37058_at
                       4
## 383 37062_at
                       4
## 384 37067_at
                      13
## 385 37079_at
                      13
## 386 37099_at
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## 387
       37109_at
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## 388 37154_at
                      13
## 389 37170_at
                       4
## 390 37172_at
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## 391
       37173_at
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## 392
       37187_at
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```

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## 393
       37206_at
## 394 37219_at
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## 395 37223_at
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## 396 37243_at
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## 397 37244_at
                      13
## 398 37280_at
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## 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
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## 406 37404_at
## 407 37416_at
                       4
## 408 37472_at
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## 409 37518_at
                      13
## 410 37520_at
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## 411 37521_s_at
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## 412 37522_r_at
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## 413 37571_at
                      13
## 414 37578_at
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## 415 37593_at
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## 416 37619_at
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## 417 37658_at
                      13
## 418 37707_i_at
                      4
## 419 37708_r_at
                      4
## 420 37723_at
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## 421 37747_at
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## 422 37748_at
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## 423 37752_at
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## 424 37757_at
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## 425 37767_at
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## 426 37840_at
                      4
## 427 37852_at
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## 428 37926_at
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## 429 37930_at
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## 430 37964_at
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## 431 38008_at
## 432 38016_at
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## 433 38024_at
                       4
## 434 38025_r_at
                       4
      38035_at
## 435
                       13
## 436 38065_at
                       4
## 437 38102_at
                       13
```

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## 438
       38120_at
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## 439 38168_at
                       4
## 440 38254_at
                        4
## 441 38304_r_at
                       13
## 442 38353_at
                       13
## 443 38375_at
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## 444 38438_at
                       4
## 445 38485_at
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## 446 38488_s_at
## 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
## 454 38715_at
                        4
## 455 38736_at
                       4
## 456 38751_i_at
                       4
## 457 38752_r_at
                       4
## 458
       38767_at
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## 459 38768_at
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## 460 38778_at
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## 461 38821_at
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## 462 38825_at
## 463 38838_at
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## 464 38854_at
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## 465
       38891_at
                        4
## 466
       38957_at
                       13
## 467
       38972_at
                       13
## 468
       38988_at
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## 469 39028_at
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## 470 39032_at
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## 471 39037_at
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## 472 39056_at
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## 473 39083_at
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## 474 39131_at
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## 475
       39132_at
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## 476 39208_i_at
## 477 39209_r_at
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## 478 39256_at
                       13
## 479 39257_at
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## 480 39269_at
                       13
## 481 39295_s_at
                       4
## 482 39333_at
                       13
```

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## 483
       39337_at
## 484 39355_at
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## 485 39369_at
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## 486 39380_at
                       4
## 487 39382_at
                       4
## 488 39469_s_at
                       13
## 489 39475_at
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## 490 39481_at
                       4
## 491 39488_at
                       13
## 492 39489_g_at
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## 493 39535_at
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## 494 39536_at
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## 495 39554_at
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## 496
      39555_at
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## 497 39576_at
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## 498 39579_at
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## 499 39600_at
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## 500 39634_at
                       4
## 501 39662_s_at
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## 502 39665_at
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## 503 39680_at
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## 504 39690_at
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## 505 39698_at
## 506 39734_at
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## 507 39746_at
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## 508 39748_at
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## 509 39758_f_at
                       13
                       13
## 510 39777_at
## 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
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## 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
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## 532 40148_at
                       4
## 533 40180_at
                       13
## 534 40181_f_at
                       13
## 535
        40199_at
                       4
## 536 40217_s_at
## 537
      40218_at
                        4
## 538 40225_at
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## 539 40226_at
                       4
## 540 40272_at
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## 541 40310_at
                        4
## 542 40312_at
                       13
## 543 40323_at
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## 544 40349_at
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## 545 40354_at
                       4
## 546 40392_at
                       13
## 547 40404_s_at
                       13
## 548 40449_at
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## 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
## 560 40711_at
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## 561 40727_at
                       4
## 562 40746_at
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## 563 40770_f_at
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## 564 40772_at
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## 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
                        4
## 572
        408_at
```

```
## 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
## 580 40993_r_at
                       4
## 581 41014_s_at
## 582 41024_f_at
                        4
## 583 41025_r_at
## 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
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## 590 41145_at
                       4
## 591 41148_at
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## 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
## 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
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## 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
                         4
          504_at
## 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
                         4
      692_s_at
## 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
                        13
        991_g_at
```

To get this in the classic named-list format:

```
z <- as.list(revmap(x)[chroms])
names(z)
## [1] "4" "13"
z[["Y"]]
## NULL</pre>
```

Many of the common methods for accessing *Bimap* objects return things in list format. This can be convenient. But you have to be careful about this if you want to use unlist(). For example the following will return multiple probes for each chromosome:

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

```
## $`12`
## [1] "1018_at" "1019_g_at" "101_at" "1021_at"
##
## $`6`
## [1] "1026_s_at" "1027_at"
```

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

```
unlist(mget(chrs, revmap(hgu95av2CHR[1:30]), ifnotfound=NA))
## 121 122 123 124 61 62
## "1018_at" "1019_g_at" "101_at" "1021_at" "1026_s_at" "1027_at"
```

Yuck! One trick that will sometimes help is to use Rfunctionunlist2. But be careful here too. Depending on what step comes next, Rfunctionunlist2 may not really help you...

```
unlist2(mget(chrs, revmap(hgu95av2CHR[1:30]), ifnotfound=NA))
## 12 12 12 12 6 6
## "1018_at" "1019_g_at" "101_at" "1021_at" "1026_s_at" "1027_at"
```

Lets ask if the probes in 'pbids' mapped to cytogenetic location "18q11.2"?

To coerce this map to a named vector:

```
pb2cyto <- as.character(x)
pb2cyto[pbids]

## <NA> <NA> <NA> <NA> <NA>
## NA NA NA NA NA NA
```

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

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

2.0.5 Accessing probes that map to multiple targets

In many probe packages, some probes are known to map to multiple genes. The reasons for this can be biological as happens in the arabidopsis packages, but usually it is due to the fact that the genome builds that chip platforms were based on were less stable than desired. Thus what may have originally been a probe designed to measure one thing can end up measuring many things. Usually you don't want to use probes like this, because if they manufacturer doesn't know what they map to then their usefullness is definitely suspect. For this reason, by default all chip packages will normally hide such probes in the standard mappings. But sometimes you may want access to the answers that the manufacturer says such a probe will map to. In such cases, you will want to use the toggleProbes method. To use this method, just call it on a standard mapping and copy the result into a new mapping (you cannot alter the original mapping). Then treat the new mapping as you would any other mapping.

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

## [1] 11471     2

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

## [1] 13426     2</pre>
```

If you then decide that you want to make a mapping that has only multiple mappings or you wish to revert one of your maps back to the default state of only showing the single mappings then you can use toggleProbes to switch back and forth.

Finally, there are also a pair of test methods hasMultiProbes and hasSingleProbes that can be used to see what methods a mapping presently has exposed.

```
## Test the multiOnly mapping
hasMultiProbes(multiOnly)

## [1] TRUE

hasSingleProbes(multiOnly)

## [1] FALSE

## Test the singleOnly mapping
hasMultiProbes(singleOnly)

## [1] FALSE

hasSingleProbes(singleOnly)

## [1] TRUE
```

2.0.6 Using SQL to access things directly

While the mapping objects provide a lot of convenience, sometimes there are definite benefits to writing a simple SQL query. But in order to do this, it is necessary to know a few things. The 1st thing you will need to know is some SQL. Fortunately, it is quite easy to learn enough basic SQL to get stuff out of a database. Here are 4 basic SQL things that you may find handy:

First, you need to know about SELECT statements. A simple example would look something like this:

```
SELECT * FROM genes;
```

Which would select everything from the genes table.

```
SELECT gene_id FROM genes;
```

Will select only the gene_id field from the genes table.

Second you need to know about WHERE clauses:

```
SELECT gene_id,_id FROM genes WHERE gene_id=1;
```

Will only get records from the genes table where the gene_id is = 1.

Thirdly, you will want to know about an inner join:

```
SELECT * FROM genes, chromosomes WHERE genes._id=chromosomes._id;
```

This is only slightly more complicated to understand. Here we want to get all the records that are in both the 'genes' and 'chromosomes' tables, but we only want ones where the '_id' field is identical. This is known as an inner join because we only want

the elements that are in both of these tables with respect to '_id'. There are other kinds of joins that are worth learning about, but most of the time, this is all you will need to do.

Finally, it is worthwhile to learn about the AS keyword which is useful for making long queries easier to read. For the previous example, we could have written it this way to save space:

```
SELECT * FROM genes AS g,chromosomes AS c WHERE g._id=c._id;
```

In a simple example like this you might not see a lot of savings from using AS, so lets consider what happens when we want to also specify which fields we want:

SELECT g.gene_id,c.chromosome FROM genes AS g,chromosomes AS c WHERE $g._id=c._id$;

Now you are most of the way there to being able to query the databases directly. The only other thing you need to know is a little bit about how to access these databases from R. With each package, you will also get a method that will print the schema for its database, you can view this to see what sorts of tables are present etc.

```
org.Hs.eg_dbschema()
```

To access the data in a database, you will need to connect to it. Fortunately, each package will automatically give you a connection object to that database when it loads.

```
org.Hs.eg_dbconn()
```

You can use this connection object like this:

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

Exercise 5

Retrieve the entrez gene ID and chromosome by using a database query. Show how you could do the same thing by using toTable

2.0.7 Combining data from multiple annotation packages at the SQL level

For a more complex example, consider the task of obtaining all gene symbols which are probed on a chip that have at least one GO BP ID annotation with evidence code IMP, IGI, IPI, or IDA. Here is one way to extract this using the environment-based packages:

```
## Obtain SYMBOLS with at least one GO BP
## annotation with evidence IMP, IGI, IPI, or IDA.
system.time({
```

```
bpids <- eapply(hgu95av2G0, function(x) {</pre>
    if (length(x) == 1 \&\& is.na(x))
       NA
    else {
         sapply(x, function(z) {
             if (z$0ntology == "BP")
               z$GOID
             else
                NA
             })
    }
})
bpids <- unlist(bpids)</pre>
bpids <- unique(bpids[!is.na(bpids)])</pre>
g2p <- mget(bpids, hgu95av2G02PR0BE)</pre>
wantedp <- lapply(g2p, function(x) {</pre>
    x[names(x) %in% c("IMP", "IGI", "IPI", "IDA")]
})
wantedp <- wantedp[sapply(wantedp, length) > 0]
wantedp <- unique(unlist(wantedp))</pre>
ans <- unlist(mget(wantedp, hgu95av2SYMBOL))</pre>
})
length(ans)
ans[1:10]
```

All of the above code could have been reduced to a single SQL query with the SQLite-based packages. But to put together this query, you would need to look 1st at the schema to know what tables are present:

```
hgu95av2_dbschema()
```

This function will give you an output of all the create table statements that were used to generate the hgu95av2 database. In this case, this is a chip package, so you will also need to see the schema for the organism package that it depends on. To learn what package it depends on, look at the ORGPKG value:

```
hgu95av20RGPKG
```

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

```
org.Hs.eg_dbschema()
```

So now we can see that we want to connect the data in the go_bp, and symbol tables from the org.Hs.eg.sqlite database along with the probes data in the hgu95av2.sqlite database. How can we do that?

It turns out that one of the great conveniences of SQLite is that it allows other databases to be 'ATTACHed'. Thus, we can keep our data in many differnt databases, and then 'ATTACH' them to each other in a modular fashion. The databases for a given build have been built together and frozen into a single version specifically to allow this sort of behavoir. To use this feature, the SQLite ATTACH command requires the filename for the database file on your filesystem. Fortunately, R provides a nice system independent way of getting that information. Note that the name of the database is always the same as the name of the package, with the suffix '.sqlite'.:

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

## Warning in rsqlite_fetch(res@ptr, n = n): Don't need to call dbFetch()
for statements, only for queries

## data frame with 0 columns and 0 rows
```

Finally, you can assemble a cross-db sql query and use the helper function as follows. Note that when we want to refer to tables in the attached database, we have to use the 'orgDB' prefix that we specified in the 'ATTACH' query above.:

Exercise 6

Retrieve the entrez gene ID, chromosome location information and cytoband infomration by using a single database query.

Exercise 7

Expand on the example in the text above to combine data from the hgu95av2.db and org.Hs.eg.db with the GO.db package so as to include the GO ID, and term definition in the output.

```
## Warning in rsqlite_fetch(res@ptr, n = n): Don't need to call dbFetch() for statements, only for queries
```

```
## Warning in rsqlite_fetch(res@ptr, n = n): Don't need to call dbFetch()
for statements, only for queries

## Warning in rsqlite_fetch(res@ptr, n = n): Don't need to call dbFetch()
for statements, only for queries

## Warning in rsqlite_fetch(res@ptr, n = n): Don't need to call dbFetch()
for statements, only for queries
```

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

```
## R version 3.4.2 (2017-09-28)
## Platform: x86_64-pc-linux-gnu (64-bit)
## Running under: Ubuntu 16.04.3 LTS
##
## Matrix products: default
## BLAS: /home/biocbuild/bbs-3.6-bioc/R/lib/libRblas.so
## LAPACK: /home/biocbuild/bbs-3.6-bioc/R/lib/libRlapack.so
##
## 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] G0.db_3.4.2
                              hgu95av2.db_3.2.3
## [3] AnnotationForge_1.20.0 org.Hs.eg.db_3.4.2
## [5] AnnotationDbi_1.40.0 IRanges_2.12.0
## [7] S4Vectors_0.16.0
                              Biobase_2.38.0
## [9] BiocGenerics_0.24.0
                              DBI_0.7
## [11] knitr_1.17
##
## loaded via a namespace (and not attached):
## [1] Rcpp_0.12.13
                       magrittr_1.5
                                      bit_1.1-12
                                                      rlang_0.1.2
## [5] stringr_1.2.0
                       blob_1.1.0
                                      highr_0.6
                                                      tools_3.4.2
## [9] htmltools_0.3.6 yaml_2.1.14
                                      bit64_0.9-7
                                                      rprojroot_1.2
## [13] digest_0.6.12 tibble_1.3.4
                                      bitops_1.0-6
                                                      RCurl_1.95-4.8
## [17] memoise_1.1.0 evaluate_0.10.1 RSQLite_2.0
                                                      rmarkdown_1.6
```

```
## [21] stringi_1.1.5 compiler_3.4.2 backports_1.1.1 XML_3.98-1.9
## [25] BiocStyle_2.6.0 pkgconfig_2.0.1
```