

Using the *GEOMETADB* package

Jack Zhu* and Sean Davis†

Genetics Branch, National Cancer Institute, National Institutes of Health

October 1, 2012

Contents

1	Overview of <i>GEOMETADB</i>	1
1.1	What is <i>GEOMETADB</i> ?	2
1.2	Conversion capabilities	2
1.3	What <i>GEOMETADB</i> is not	2
2	Getting Started	4
2.1	Getting the <i>GEOMETADB</i> database	4
2.2	A word about SQL	5
3	Examples	5
3.1	Interacting with the database	5
3.2	Writing SQL queries and getting results	7
3.3	Conversion of GEO entity types	10
3.4	Mappings between GPL and Bioconductor microarray annotation packages . .	11
3.5	More advanced queries	12

1 Overview of *GEOMETADB*

The NCBI Gene Expression Omnibus (GEO) represents the largest repository of microarray data in existence. One difficulty in dealing with GEO is finding the microarray data that is of interest. As part of the NCBI Entrez search system, GEO can be searched online via web pages or using NCBI Eutils. However, the web search is not as full-featured as it could be, particularly for programmatic access. NCBI Eutils offers another option for finding data within the vast stores of GEO, but it is cumbersome to use, often requiring multiple

*zhujack@mail.nih.gov

†sdavis2@mail.nih.gov

complicated Eutils calls to get at the relevant information. We have found it **absolutely critical** to have ready access not just to the microarray data, but to the metadata describing the microarray experiments. To this end we have created *GEOMETADB*.

1.1 What is *GEOMETADB*?

The *GEOMETADB* is an attempt to make querying the metadata describing microarray experiments, platforms, and datasets both easier and more powerful. At the heart of *GEOMETADB* is a SQLite database that stores nearly all the metadata associated with all GEO data types including GEO samples (GSM), GEO platforms (GPL), GEO data series (GSE), and curated GEO datasets (GDS), as well as the relationships between these data types. This database is generated by our server by parsing all the records in GEO and needs to be downloaded via a simple helper function to the user's local machine before *GEOMETADB* is useful. Once this is done, the entire GEO database is accessible with simple SQL-based queries. With the *GEOMETADB* database, queries that are simply not possible using NCBI tools or web pages are often quite simple. The relationships between the tables in the *GEOMETADB* SQLite database can be seen in figure 1.

1.2 Conversion capabilities

A very typical problem for large-scale consumers of GEO data is to determine the relationships between various GEO accession types. As examples, consider the following questions:

- What samples are associated with GEO platform “GPL96”, which represents the Affymetrix hgu133a array?
- What GEO Series were performed using “GPL96”?
- What samples are in my favorite three GEO Series records?
- How many samples are associated with the ten most popular GEO platforms?

Because these types of questions are common, *GEOMETADB* contains the function `geoConvert` that addresses these questions directly and efficiently.

1.3 What *GEOMETADB* is not

We have faithfully parsed and maintained in GEO when creating *GEOMETADB*. This means that limitations inherent to GEO are also inherent in *GEOMETADB*. We have made no attempt to curate, semantically recode, or otherwise “clean up” GEO; to do so would require significant resources, which we do not have.

GEOMETADB does not contain any microarray data. For access to microarray data from within R/Bioconductor, please look at the *GEOquery* package. In fact, we would expect that many users will find that the combination of *GEOMETADB* and *GEOquery* is quite powerful.

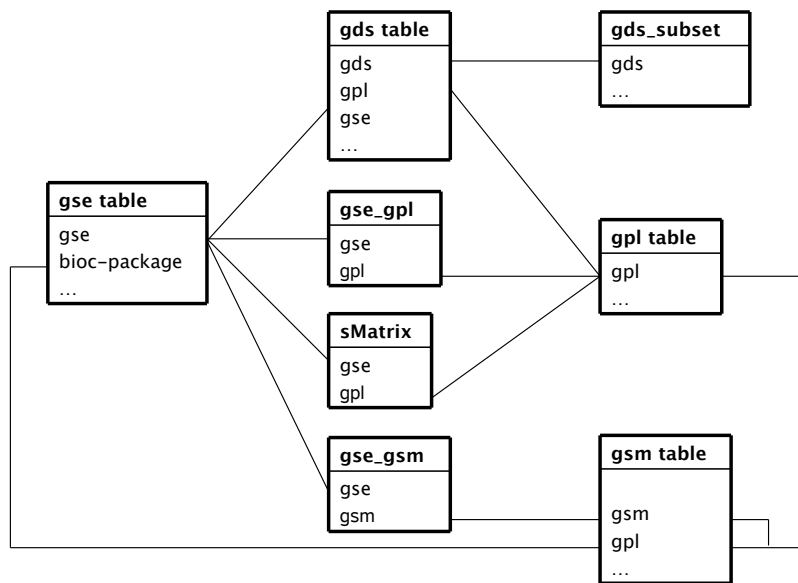


Figure 1: A graphical representation (sometimes called an *Entity-Relationship Diagram*) of the relationships between the tables in the GEOmetadb SQLite database

2 Getting Started

Once *GEOmetadb* is installed (see the Bioconductor website for full installation instructions), we are ready to begin.

2.1 Getting the *GEOmetadb* database

This package does not come with a pre-installed version of the database. This has the advantage that the user will get the most up-to-date version of the database to start; the database can be re-downloaded using the same command as often as desired. First, load the library.

```
> library(GEOmetadb)
```

The download and uncompress steps are done automatically with a single command, `getSQLiteFile`.

```
> getSQLiteFile()
```

Unzipping...

Metadata associate with downloaded file:

	name	value
1	schema version	1.0
2	creation timestamp	2012-09-29 02:15:00
[1]	"D:/biocbld/bbs-2.11-bioc/tmpdir/RtmpeQhV1b/Rbuild35c451a0e38/GEOmetadb/inst/doc/GEOmetadb.sqlite"	

The default storage location is in the current working directory and the default filename is “GEOmetadb.sqlite”; it is best to leave the name unchanged unless there is a pressing reason to change it.

Since this SQLite file is of key importance in *GEOmetadb*, it is perhaps of some interest to know some details about the file itself.

```
> file.info('GEOmetadb.sqlite')
```

	size	isdir	mode	mtime	ctime	atime	exe
GEOmetadb.sqlite	2091419648	FALSE	666				
GEOmetadb.sqlite	2012-10-01 23:48:26						
GEOmetadb.sqlite	2012-10-01 23:48:13						
GEOmetadb.sqlite	2012-10-01 23:48:13		no				

Now, the SQLite file is available for connection. The standard *DBI* functionality as implemented in *RSQLite* function `dbConnect` makes the connection to the database. The `dbDisconnect` function disconnects the connection.

```
> con <- dbConnect(SQLite(), 'GEOmetadb.sqlite')
> dbDisconnect(con)
```

```
[1] TRUE
```

The variable `con` is an *RSQLite* connection object.

2.2 A word about SQL

The Structured Query Language, or SQL, is a very powerful and standard way of working with relational data. GEO is composed of several data types, all of which are related to each other; in fact, NCBI uses a relational SQL database for metadata storage and querying. SQL databases and SQL itself are designed specifically to work efficiently with just such data. While the goal of many programming projects and programmers is to hide the details of SQL from the user, we are of the opinion that such efforts may be counterproductive, particularly with complex data and the need for *ad hoc* queries, both of which are characteristics with GEO metadata. We have taken the view that exposing the power of SQL will enable users to maximally utilize the vast data repository that is GEO. We understand that many users are not accustomed to working with SQL and, therefore, have devoted a large section of the vignette to working examples. Our goal is not to teach SQL, so a quick tutorial of SQL is likely to be beneficial to those who have not used it before. Many such tutorials are available online and can be completed in 30 minutes or less.

3 Examples

3.1 Interacting with the database

The functionality covered in this section is covered in much more detail in the *DBI* and *RSQLite* package documentation. We cover enough here only to be useful.

Again, we connect to the database.

```
> con <- dbConnect(SQLite(), 'GEOmetadb.sqlite')
```

The `dbListTables` function lists all the tables in the SQLite database handled by the connection object `con`.

```
> geo_tables <- dbListTables(con)
> geo_tables

[1] "gds"                "gds_subset"
[3] "geoConvert"         "geodb_column_desc"
[5] "gpl"                "gse"
[7] "gse_gpl"            "gse_gsm"
[9] "gsm"                "metaInfo"
[11] "sMatrix"
```

There is also the `dbListFields` function that can list database fields associated with a table.

```
> dbListFields(con, 'gse')
```

```
[1] "ID"                "title"
[3] "gse"               "status"
[5] "submission_date"   "last_update_date"
[7] "pubmed_id"         "summary"
[9] "type"              "contributor"
[11] "web_link"          "overall_design"
[13] "repeats"           "repeats_sample_list"
[15] "variable"          "variable_description"
[17] "contact"           "supplementary_file"
```

Sometimes it is useful to get the actual SQL schema associated with a table. As an example of doing this and using an *RSQLite* shortcut function, `sqliteQuickSQL`, we can get the table schema for the *gpl* table.

```
> sqliteQuickSQL(con, 'PRAGMA TABLE_INFO(gpl)')
```

	cid		name	type	notnull	dflt_value	pk
1	0		ID	REAL	0	<NA>	0
2	1		title	TEXT	0	<NA>	0
3	2		gpl	TEXT	0	<NA>	0
4	3		status	TEXT	0	<NA>	0
5	4		submission_date	TEXT	0	<NA>	0
6	5		last_update_date	TEXT	0	<NA>	0
7	6		technology	TEXT	0	<NA>	0
8	7		distribution	TEXT	0	<NA>	0
9	8		organism	TEXT	0	<NA>	0
10	9		manufacturer	TEXT	0	<NA>	0
11	10		manufacture_protocol	TEXT	0	<NA>	0
12	11		coating	TEXT	0	<NA>	0
13	12		catalog_number	TEXT	0	<NA>	0
14	13		support	TEXT	0	<NA>	0
15	14		description	TEXT	0	<NA>	0
16	15		web_link	TEXT	0	<NA>	0
17	16		contact	TEXT	0	<NA>	0
18	17		data_row_count	REAL	0	<NA>	0
19	18		supplementary_file	TEXT	0	<NA>	0
20	19		bioc_package	TEXT	0	<NA>	0

5 GSE7882
6 GSE8486
7 GSE9328
8 GSE14543
9 GSE15621
10 GSE16087
11 GSE16088
12 GSE16091
13 GSE16102
14 GSE18544
15 GSE19063
16 GSE20016
17 GSE25164
18 GSE22520
19 GSE25127
20 GSE29428

1
2 Gene expression profiling of CD4+ T-cells an
3
4 Detection of novel ampl
5 Gene Expression and Comparative Genomic Hybridization of Duct
6 Whole genome DNase hype
7
8 A molecular
9 Acute Lymphocytic Leu
10 Gene expressi
11 Gene express
12 Gene expression pr
13 Gene expression profile
14 Expression Profiling of a Mouse Xenograft Model of "Triple-Negative" Breast Canc
15 Genome-wide map of PAX3-FKHR
16 Analyses of Human Brain Metastases of Breast Cancer Reveal the Association between HK
17
18 Mouse Models of Alveolar/Embryonal Rhabdo
19 Ewing Sarcoma c
20 A methyl-deviator epigenotype of estrogen-receptor-positive breast carcinoma is

As another example, GEOmetadb can find all samples on GPL96 (Affymetrix hgu133a) that have .CEL files available for download.

```
> rs <- dbGetQuery(con,paste("select gsm,supplementary_file",
+                             "from gsm where gpl='GPL96'",
```



```
+                                "and supplementary_file like '%CEL.gz'"))
> dim(rs)
```

```
[1] 21975      2
```

But why limit to only GPL96? Why not look for all Affymetrix arrays that have .CEL files? And list those with their associated GPL information, as well as the Bioconductor annotation package name?

```
> rs <- dbGetQuery(con,paste("select gpl.bioc_package,gsm.gpl,",
+                             "gsm,gsm.supplementary_file",
+                             "from gsm join gpl on gsm.gpl=gpl.gpl",
+                             "where gpl.manufacturer='Affymetrix'",
+                             "and gsm.supplementary_file like '%CEL.gz' "))
> rs[1:5,]
```

	bioc_package	gpl	gsm	supplementary_file
1	hu6800	GPL80	GSM575	ftp://ftp.ncbi.nih.gov/pub/geo/DATA/supplementary/samples/GSMnnn/GSM575/GSM575.cel.gz
2	hu6800	GPL80	GSM576	ftp://ftp.ncbi.nih.gov/pub/geo/DATA/supplementary/samples/GSMnnn/GSM576/GSM576.cel.gz
3	hu6800	GPL80	GSM577	ftp://ftp.ncbi.nih.gov/pub/geo/DATA/supplementary/samples/GSMnnn/GSM577/GSM577.cel.gz
4	hu6800	GPL80	GSM578	ftp://ftp.ncbi.nih.gov/pub/geo/DATA/supplementary/samples/GSMnnn/GSM578/GSM578.cel.gz
5	hu6800	GPL80	GSM579	ftp://ftp.ncbi.nih.gov/pub/geo/DATA/supplementary/samples/GSMnnn/GSM579/GSM579.cel.gz

Of course, we can combine programming and data access. A simple `sapply` example shows how to query each of the tables for number of records.

```
> getTableCounts <- function(tableName,conn) {
+   sql <- sprintf("select count(*) from %s",tableName)
+   return(dbGetQuery(conn,sql)[1,1])
+ }
> do.call(rbind,sapply(geo_tables,getTableCounts,con,simplify=FALSE))
```

	[,1]
gds	2721
gds_subset	15275
geoConvert	3565064
geodb_column_desc	104
gpl	10722

<code>gse</code>	32661
<code>gse_gpl</code>	38459
<code>gse_gsm</code>	894949
<code>gsm</code>	765310
<code>metaInfo</code>	2
<code>sMatrix</code>	39186

3.3 Conversion of GEO entity types

Large-scale consumers of GEO data might want to convert GEO entity type from one to others, e.g. finding all GSM and GSE associated with 'GPL96'. Function `geoConvert` does the conversion with a very fast mapping between entity types.

Covert 'GPL96' to other possible types in the `GEOmetadb.sqlite`.

```
> conversion <- geoConvert('GPL96')
```

Check what GEO types and how many entities in each type in the conversion.

```
> lapply(conversion, dim)
```

```
$gse
[1] 932  2
```

```
$gsm
[1] 31484  2
```

```
$gds
[1] 325  2
```

```
$sMatrix
[1] 983  2
```

```
> conversion$gse[1:5,]
```

	from_acc	to_acc
1	GPL96	GSE1000
2	GPL96	GSE10024
3	GPL96	GSE10043
4	GPL96	GSE10072
5	GPL96	GSE10089

```
> conversion$gsm[1:5,]
```

```

      from_acc      to_acc
1      GPL96 GSM100386
2      GPL96 GSM100454
3      GPL96 GSM100455
4      GPL96 GSM100456
5      GPL96 GSM100457

> conversion$gds[1:5,]

```

```

      from_acc      to_acc
1      GPL96 GDS1023
2      GPL96 GDS1036
3      GPL96 GDS1050
4      GPL96 GDS1062
5      GPL96 GDS1063

> conversion$sMatrix[1:5,]

```

```

      from_acc                                     to_acc
1      GPL96 GSE1000_series_matrix.txt.gz
2      GPL96 GSE10024_series_matrix.txt.gz
3      GPL96 GSE10043_series_matrix.txt.gz
4      GPL96 GSE10072_series_matrix.txt.gz
5      GPL96 GSE10089_series_matrix.txt.gz

```

3.4 Mappings between GPL and Bioconductor microarray annotation packages

The function `getBiocPlatformMap` is to get GPL information of a given list of Bioconductor microarray annotation packages. Note currently the `GEOmetadb` does not contains all the mappings, but we are trying to construct a relative complete list.

Get GPL information of 'hgu133a' and 'hgu95av2':

```

> getBiocPlatformMap(con, bioc=c('hgu133a', 'hgu95av2'))

                                     title      gpl
1 [HG-U133A] Affymetrix Human Genome U133A Array GPL96
2 [HG-U95A] Affymetrix Human Genome U95A Array GPL91
      bioc_package manufacturer      organism
1      hgu133a      Affymetrix Homo sapiens
2      hgu95av2      Affymetrix Homo sapiens
      data_row_count
1              22283
2              12626

```

3.5 More advanced queries

Now, for something a bit more complicated, we would like to find all the human breast cancer-related Affymetrix gene expression GEO series.

```
> sql <- paste("SELECT DISTINCT gse.title,gse.gse",
+             "FROM",
+             " gsm JOIN gse_gsm ON gsm.gsm=gse_gsm.gsm",
+             " JOIN gse ON gse_gsm.gse=gse.gse",
+             " JOIN gse_gpl ON gse_gpl.gse=gse.gse",
+             " JOIN gpl ON gse_gpl.gpl=gpl.gpl",
+             "WHERE",
+             " gsm.molecule_ch1 like '%total RNA%' AND",
+             " gse.title LIKE '%breast cancer%' AND",
+             " gpl.organism LIKE '%Homo sapiens%'",sep=" ")
> rs <- dbGetQuery(con,sql)
> dim(rs)

[1] 391  2

> print(rs[1:5,],right=FALSE)

  title
1 Breast Cancer aCGH
2 Human mammary epithelium and breast cancer
3 Cell-type specific responses to chemotherapeutics in breast cancer
4 E2 and SERM Treatment of MCF-7 Breast Cancer Cells
5 Estradiol Treated Breast Cancer Cells Expressing Mutant Estrogen Receptors
  gse
1 GSE3281
2 GSE53
3 GSE763
4 GSE848
5 GSE1045
```

Finally, it is probably a good idea to close the connection, please see *DBI* for detail.

```
> dbDisconnect(con)
```

```
[1] TRUE
```

If you want to remove old `GEOmetadb.sqlite` file before retrieve a new version from the server, execute the following codes:

```
> file.remove('GEOmetadb.sqlite')
```

```
[1] TRUE
```