poplite vignette

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1 Introduction

Prior to utilizing a given database in a research context, it has to be designed, scripts written to format existing data to fit into the tables, and the data has to be loaded. The loading can be as simple as just inserting data into a given table or in addition it may need to respect columns from other tables. The poplite package was developed originally to simplify the process of population and management of SQLite databases using R. It provides a schema object and corresponding methods which allows a user to easily understand the database structure as well as extend or modify it. The database can be populated using this schema and the user can specify both raw data and a transformational function to apply prior to loading. This functionality facilitates loading of large, non-data.frame type objects as is demonstrated below in the 'VCF Database' section. It has since also incorportated and extended functionality from the dplyr package [Wickham and Francois, 2014] to provide a convienient query interface using dplyr's verbs. Notably, cross table queries can be carried out automatically using the specified schema object.

2 Sample Tracking Database

We will start by working through a simple example that illustrates how to use poplite for many common database tasks. Here we will create a sample tracking database for DNA specimens collected on patients in a clinical research setting. Our example is a set of 3 data.frames which consists of randomly generated values resembling commonly collected data. We first load the package and the example data, going through each data.frame in turn.

2.1 Database Population

```
> library(poplite)
> data(clinical)
> ls()
[1] "clinical" "dna" "samples"
```

The clinical data.frame contains information on a group of patients including sex, age, disease status as well as other variables/covariates.

> head(clinical)

```
sample_id sex age status var_wave_1
                                         var_wave_2
                 12
                            0.7567748
                                         0.26783502
1
          1
              Μ
2
          2
              F
                  7
                          0 -1.7267304
                                        0.65325768
3
          3
              М
                 18
                          1 -0.6015067 -0.12270866
4
                  13
                          1 -0.3520465 -0.41367651
```

The samples data.frame records whether a given patient, keyed by sample_id was observed in one of several 'waves' and whether they contributed a DNA sample.

> head(samples)

```
sample_id wave did_collect
1
            1
                  1
2
            1
                  2
                                 N
            2
                                 Y
3
                  1
4
            2
                  2
                                 N
5
            3
                  1
                                 N
6
            3
                  2
                                 Y
```

The dna data.frame provides some information (concentration in nanograms/microliter) on the DNA specimen collected from a given patient during a given wave.

> head(dna)

```
sample_id wave lab_id
                                 ng.ul
           1
                 1 dna_1_1 294.614119
1
3
           2
                 1 dna_2_1
                              5.777775
6
           3
                 2 dna_3_2 203.292147
10
           5
                 2 dna_5_2 158.137716
12
           6
                 2 dna_6_2 167.162274
15
                 1 dna_8_1 183.204669
```

As these data are already in table form, loading them should be relatively straightforward. The first step is the creation of a schema object of class TableSchemaList whose name is descriptive of the data therein. For data.frames a convenience function (makeSchemaFromData) is provided which does some basic checks and creates an appropriate table based on the column names and inferred types.

```
> sample.tracking <- makeSchemaFromData(clinical, "clinical")
> sample.tbsl <- makeSchemaFromData(samples, "samples")
> sample.tracking <- append(sample.tracking, sample.tbsl)
> try(dna.tbsl <- makeSchemaFromData(dna, "dna"))
>
```

The error caused by attempting to create a schema object from the 'dna' data.frame, is due to the formatting of the column name of 'ng.ul' which is a valid R name, but not a valid SQLite name. A convienient way to fix this is to use the correct.df.names function as below. Note that this modified data.frame will be the one that has to be provided to the populate method.

```
> new.dna <- correct.df.names(dna)
> dna.tbsl <- makeSchemaFromData(new.dna, "dna")
> sample.tracking <- append(sample.tracking, dna.tbsl)
>
```

At this point, the database can be created and populated using the schema defined in 'sample.tracking' and the data present in the respective data.frames. However, this requires anyone who wants to query across the tables be able to determine the relationships between the tables. In some cases this can be determined by column names alone, in other cases it may not be so clear. The poplite package allows the specification

of relationships between tables using the R formula syntax. This functionality is probably best illustrated by example.

The 'clinical' table is the starting point of this database as both the 'samples' and 'dna' tables refer back to it. In the case of both the 'samples' and 'dna' tables, the 'clinical' table can be referred to using the 'sample_id' column. In addition, the 'dna' table can be referred to by the 'samples' table using a combination of 'sample_id' and 'wave' and vice versa. These types of relationship can be created by the following:

```
> relationship(sample.tracking, from="clinical", to="samples") <- sample_id~sample_id
> relationship(sample.tracking, from="clinical", to="dna") <-sample_id~sample_id
> relationship(sample.tracking, from="samples", to="dna") <- sample_id+wave~sample_id+wave</pre>
```

Now that our schema is complete, we are now ready to populate our database. First, we create a Database object which simply contains both the schema as well as the file path to where the database resides. We then call the populate method and provide it with our named data.frames.

```
> sample.tracking.db <- Database(sample.tracking, tempfile())
> populate(sample.tracking.db, dna=new.dna, samples=samples, clinical=clinical)
>
```

2.2 Querying

As mentioned in the introduction, the query interface utilizes the approach of the dplyr package, whereby a small set of verbs are used to perform common queries. In addition to utilizing the single table verbs defined in dplyr, poplite defines multi-table versions of the select and filter verbs. The select verb allows the user to select columns from a table-like object, in this case an SQLite database. As the poplite version of select and filter can be used for any of the tables in the defined schema, the most important requirement is for the user to make sure the column(s) are unambigous in terms of the tables. This can be done in several ways:

(1) Only for the select statement, the .tables argument allows selecting all or part of the columns of a given table(s). If multiple tables are provided, then they are first joined (an 'inner join' in SQL terminology) using the specified relationships in the schema. This provides a convienent way to retrieve a combined version of the data in the database.

```
> select(sample.tracking.db, .tables="dna")
            table<dna> [?? x 5]
# Source:
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
   dna_ind sample_id wave
                              lab_id
                                          ng_ul
     <int>
               <int> <int>
                               <chr>
                                           <dbl>
 1
         1
                    1
                          1 dna_1_1 294.614119
         2
                    2
 2
                          1 dna_2_1
                                       5.777775
 3
         3
                    3
                          2
                            dna_3_2 203.292147
 4
         4
                   5
                          2
                             dna_5_2 158.137716
 5
         5
                    6
                          2
                             dna_6_2 167.162274
 6
         6
                   8
                          1
                             dna_8_1 183.204669
 7
         7
                   9
                          1
                             dna_9_1 96.772302
 8
         8
                   9
                          2
                             dna_9_2 113.345676
 9
         9
                  10
                          1 dna_10_1
                                      46.179612
10
        10
                  15
                          1 dna_15_1
                                      40.964460
# ... with more rows
> select(sample.tracking.db, sample_id:lab_id, .tables="dna")
```

lazy query [?? x 3]

Source:

Database: sqlite 3.19.3

```
[/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
   sample_id wave
                      lab id
       <int> <int>
                       <chr>
           1
                 1 dna_1_1
 1
           2
 2
                 1 dna_2_1
 3
           3
                 2 dna_3_2
 4
           5
                 2 dna 5 2
 5
           6
                 2 dna_6_2
 6
           8
                 1
                    dna_8_1
 7
           9
                 1 dna_9_1
 8
           9
                 2 dna_9_2
9
                 1 dna_10_1
          10
10
          15
                 1 dna_15_1
# ... with more rows
> select(sample.tracking.db, .tables=c("clinical","dna"))
# Source:
            lazy query [?? x 11]
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
                                   age status var_wave_1 var_wave_2 dna_ind
   clinical_ind sample_id
                            sex
          <int>
                    <int> <chr> <int> <int>
                                                    <dbl>
                                                                <dbl>
                                                                         <int>
 1
                         1
                                    12
                                            0 0.7567748 0.26783502
                                                                             1
 2
              2
                         2
                               F
                                     7
                                            0 -1.7267304 0.65325768
                                                                             2
 3
              3
                         3
                               М
                                    18
                                            1 -0.6015067 -0.12270866
                                                                             3
 4
              5
                         5
                               F
                                     7
                                            1 0.7035239 -2.64314895
                                                                             4
 5
              6
                         6
                               М
                                     8
                                            0 -0.1056713 -0.09294102
                                                                             5
 6
              8
                        8
                               F
                                    18
                                            0 1.6844357 0.53539884
                                                                             6
 7
              9
                         9
                               F
                                    20
                                            1 0.9113913 -0.55527835
                                                                             7
                         9
                               F
 8
              9
                                    20
                                                                             8
                                            1 0.9113913 -0.55527835
 9
             10
                       10
                                    12
                                            1 0.2374303 1.77950291
                               Μ
                                                                             9
                               F
                                            0 0.6837455 -0.45033862
10
             14
                       15
                                     3
                                                                            10
# ... with more rows, and 3 more variables: wave <int>, lab_id <chr>,
    ng_ul <dbl>
(2) If a column or set of columns uniquely identifies a table, then no further information is needed to execute
the query.
> select(sample.tracking.db, sample_id:lab_id)
# Source:
            lazy query [?? x 3]
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
   sample_id wave
                     lab id
       <int> <int>
                       <chr>
           1
                    dna_1_1
 1
                 1
           2
 2
                    dna_2_1
                 1
 3
           3
                 2
                    dna_3_2
 4
           5
                 2 dna_5_2
 5
           6
                 2 dna_6_2
 6
           8
                 1 dna_8_1
 7
           9
                 1 dna_9_1
           9
8
                 2 dna_9_2
9
          10
                 1 dna_10_1
```

1 dna_15_1

10

15

```
# ... with more rows
> head(filter(sample.tracking.db, sex == "M" & var_wave_1 > 0))
            lazy query [?? x 7]
# Source:
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
  clinical_ind sample_id
                                   age status var_wave_1 var_wave_2
                             sex
         <int>
                    <int> <chr> <int> <int>
                                                     <dbl>
1
              1
                        1
                               Μ
                                    12
                                             0 0.75677476 0.2678350
2
             10
                       10
                                    12
                               М
                                             1 0.23743027 1.7795029
3
             12
                       13
                               Μ
                                     5
                                             0 0.66082030 1.2722668
4
                                             1 0.00729009 -1.4385066
             18
                       19
                               Μ
                                     6
                                             0 1.01755864 -0.1905168
5
             19
                       20
                               М
                                    12
             21
                       23
                               М
                                    18
                                             1 1.51921771 -1.0056363
6
> filter(sample.tracking.db, sample_id == 97 & var_wave_1 > 0)
            lazy query [?? x 7]
# Source:
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
  clinical_ind sample_id
                             sex
                                   age status var_wave_1 var_wave_2
                                                     <dbl>
         <int>
                    <int> <chr> <int> <int>
                                                                 <dbl>
1
            85
                       97
                                             1 0.7564064 -2.070751
Whereas the following fails because 'sample_id' is defined in several tables.
> try(filter(sample.tracking.db, sample_id == 97))
(3) A table can be specified in the query using a '.' similar to how it is done in SQL, i.e. tableX.ColumnY.
This only should be done once per statement for select statements, but per variable for filter statements
as is shown below. This restriction reflects how the queries are carried out. Each grouping of statements
statements are applied to the specified or inferred table prior to joining. Note that for the poplite filter
verb cross-table 'OR' statements are currently not supported.
> select(sample.tracking.db, dna.sample_id)
# Source:
            lazy query [?? x 1]
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
   sample_id
       <int>
1
           1
 2
           2
 3
           3
 4
           5
 5
           6
 6
           8
 7
           9
 8
           9
9
          10
10
          15
# ... with more rows
```

> select(sample.tracking.db, dna.sample_id:lab_id)

```
# Source:
            lazy query [?? x 3]
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
   sample_id wave
                     lab_id
       <int> <int>
                      <chr>>
                 1 dna_1_1
 1
           1
 2
           2
                 1 dna 2 1
                 2 dna_3_2
 3
           3
                 2 dna_5_2
 4
           5
 5
           6
                 2 dna_6_2
 6
           8
                 1 dna_8_1
 7
           9
                 1 dna_9_1
           9
 8
                 2 dna_9_2
9
                 1 dna_10_1
          10
10
          15
                 1 dna_15_1
# ... with more rows
> filter(sample.tracking.db, clinical.sample_id == 97)
# Source:
            lazy query [?? x 7]
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
  clinical_ind sample_id
                                 age status var_wave_1 var_wave_2
                           sex
         <int>
                   <int> <chr> <int> <int> <int>
                                                  <dbl>
                                                             <dbl>
            85
                             М
                                           1 0.7564064 -2.070751
> filter(sample.tracking.db, clinical.status == 1 & dna.wave==2)
# Source:
           lazy query [?? x 11]
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc66576b2a8]
   clinical_ind sample_id
                            sex
                                   age status var_wave_1 var_wave_2 dna_ind
          <int>
                    <int> <chr> <int> <int>
                                                    <dbl>
                                                                 <dbl>
                                                                         <int>
 1
              3
                        3
                              М
                                   18
                                            1 -0.60150671 -0.12270866
                                                                             3
 2
              5
                              F
                                            1 0.70352390 -2.64314895
                        5
                                    7
                                                                             4
 3
              9
                        9
                              F
                                   20
                                            1 0.91139129 -0.55527835
                                                                             8
 4
             18
                       19
                              Μ
                                    6
                                            1 0.00729009 -1.43850664
                                                                            14
 5
             20
                       21
                              F
                                   15
                                            1 -1.18843404 0.37842390
                                                                            18
 6
             21
                       23
                                   18
                                            1 1.51921771 -1.00563626
                                                                            22
 7
             22
                       24
                                    15
                                            1 0.37738797 0.01925927
                                                                            24
                              М
 8
             24
                       27
                              Μ
                                     8
                                            1 -0.20078102 1.08477509
                                                                            28
9
             28
                       32
                              М
                                     2
                                            1 1.67105483 0.65990264
                                                                            34
10
             29
                       33
                              F
                                     5
                                            1 0.05601673 -0.19988983
                                                                            35
 ... with more rows, and 3 more variables: wave <int>, lab_id <chr>,
#
   ng_ul <dbl>
>
```

The poplite query interface is 'opt-in', meaning that more complex queries can always be carried out directly using the methodology provided in the dplyr package or plain SQL statements after first connecting to the database file using RSQLite. Below are three approaches of performing the same query:

```
> #poplite + dplyr
> wave.1.samp.pop <- filter(select(sample.tracking.db, .tables=c("samples", "dna")), wave == 1)
> #dplyr
> src.db <- src_sqlite(dbFile(sample.tracking.db), create = F)
> samp.tab <- tbl(src.db, "samples")</pre>
```

```
> dna.tab <- tbl(src.db, "dna")
> wave.1.samp.dplyr <- inner_join(filter(samp.tab, wave == 1), dna.tab,
+ by=c("sample_id", "wave"))
> library(RSQLite)
> #RSQLite
> samp.db <- dbConnect(SQLite(), dbFile(sample.tracking.db))
> wave.1.samp.sql <- dbGetQuery(samp.db, 'SELECT * FROM samples JOIN dna
+ USING (sample_id, wave) WHERE wave == 1')
> dbDisconnect(samp.db)
> all.equal(as.data.frame(wave.1.samp.pop), wave.1.samp.sql)
[1] TRUE
> all.equal(as.data.frame(wave.1.samp.dplyr), wave.1.samp.sql)
[1] TRUE
```

2.3 Additional Features

Instead of directly cross referencing columns as we did for the database above in our relationships (e.g. sample_id - sample_id) we can also specify that we instead want to use the 'primary key' of a given table instead of one or more columns. Where the primary key is a column of integer values that uniquely identifies each row and by default it was added automatically by makeSchemaFromData. This approach is commonly used for lookup tables, for instance say we wanted a seperate table for gender and to only maintain an integer value specifying whether a patient was male, female or unknown for the clinical table. We could do this as follows where '.' is a shortcut that indicates that the primary key for the table should be used:

```
> gender <- data.frame(sex=unique(clinical$sex), stringsAsFactors=F)</pre>
> gend.tbsl <- makeSchemaFromData(gender, "gender")</pre>
> sample.tracking <- append(gend.tbsl, sample.tracking)</pre>
> relationship(sample.tracking, from="gender", to="clinical") <- .~sex
> sample.tracking.db <- Database(sample.tracking, tempfile())</pre>
> populate(sample.tracking.db, dna=new.dna, samples=samples, clinical=clinical, gender=gender)
> select(sample.tracking.db, .tables="gender")
            table<gender> [?? x 2]
# Source:
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc67da87665]
  gender_ind
               sex
       <int> <chr>
                 M
1
           1
2
> head(select(sample.tracking.db, .tables="clinical"))
# Source:
            lazy query [?? x 7]
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc67da87665]
  clinical_ind sample_id
                            age status var_wave_1 var_wave_2 gender_ind
         <int>
                    <int> <int>
                                <int>
                                             <dbl>
                                                         <dbl>
                                                                     <int>
                        1
                             12
                                     0 0.7567748 0.26783502
                                                                         1
1
             1
2
             2
                        2
                              7
                                     0 -1.7267304 0.65325768
                                                                         2
                        3
3
             3
                             18
                                     1 -0.6015067 -0.12270866
                                                                         1
4
             4
                        4
                                     1 -0.3520465 -0.41367651
                             13
                                                                         1
```

```
5
                                         0.7035239 -2.64314895
6
              6
                               8
                                       0 -0.1056713 -0.09294102
> select(sample.tracking.db, .tables=c("clinical", "gender"))
# Source:
             lazy query [?? x 8]
# Database: sqlite 3.19.3
    [/private/var/folders/xf/6sc0vfxj5dj4_0dt0r9jm_jdnrv5h3/T/RtmppH1Iyz/file3dc67da87665]
   clinical_ind sample_id
                              age status var_wave_1 var_wave_2 gender_ind
           <int>
                     <int> <int>
                                    <int>
                                                <dbl>
                                                             <dbl>
                                                                         <int> <chr>
 1
               1
                          1
                               12
                                        0
                                           0.7567748
                                                       0.26783502
                                                                             1
                                                                                   Μ
 2
               2
                          2
                                7
                                        0 -1.7267304
                                                       0.65325768
                                                                             2
                                                                                   F
 3
               3
                          3
                               18
                                        1 -0.6015067 -0.12270866
                                                                             1
                                                                                   М
 4
               4
                          4
                               13
                                        1 -0.3520465 -0.41367651
                                                                                   M
                                                                             1
 5
               5
                          5
                                                                             2
                                7
                                           0.7035239 -2.64314895
                                                                                   F
 6
               6
                          6
                                8
                                        0 -0.1056713 -0.09294102
                                                                             1
                                                                                   Μ
 7
               7
                          7
                                4
                                          -1.2586486
                                                       0.43028470
                                                                             1
                                                                                   Μ
 8
               8
                          8
                                                                             2
                                                                                   F
                               18
                                           1.6844357
                                                       0.53539884
 9
               9
                          9
                               20
                                           0.9113913 -0.55527835
                                                                             2
                                                                                   F
              10
10
                         10
                               12
                                           0.2374303
                                                      1.77950291
                                                                                   М
      with more rows
>
```

It is important to note that currently specifying a relationship between two tables in this manner will result in the 'to' table being limited to only those values in common between the specified columns in the two tables. So do not use this approach unless you expect that the two tables are consistent with each other.

3 Variant Call Format Database

One of the the most useful features of poplite is that databases can be created from any R object that can be coerced to a data.frame and they can be populated iteratively. This more complex example involves the parsing and loading of a variant call format (VCF) file. This type of file was devised to encode DNA variations from a reference genome for a given set of samples. In addition, it can also provide numerical summaries on the confidence that the variant exists as well as other summary stats and annotations. For more details, see the following specifications: http://ga4gh.org/#/fileformats-team. As parsing is already provided by the VariantAnnotation package [Obenchain et al., 2014] in Bioconductor [Gentleman et al., 2004], we will focus on the population of a database using this data. We will use the example dataset from the VariantAnnotation package and read it into memory as a VCF object as shown in the VariantAnnotation vignette.

The first table we will create is a representation of the chromosome, location and reference positions where at least one variant was observed. To do this we will create a function that takes a VCF object as input and returns a data.frame. This function and a subset of the VCF object is passed to the makeSchemaFromFunction helper function. What this helper function does is execute the desired function on the provided VCF object, determine the table structure from the returned data.frame and package the results in a TableSchemaList object. It is important that the name(s) for the input objects match between the provided function, makeSchemaFromFunction and ultimately populate.

```
+ stringsAsFactors=FALSE
+ )
+ return(ref.dta)
+ }
> vcf.sc <- makeSchemaFromFunction(populate.ref.table, "reference", vcf.obj=vcf[1:5])
>
```

Each variant position in our 'reference' table can have multiple alternatives (termed alleles) which were determined by the genotyping program which generated the VCF file. The 'alleles' table can be formed as follows:

Finally we can form a table that records the number of alternative alleles for each sample. Implementation Note: the 'allele_count' column is very simple due to fact that this example dataset only contains one alternative allele for each variant. Multi-alleleic cases would have to be dealt with differently as we would need to be sure that the appropriate allele was counted for each genotype.

```
> populate.samp.alt.table <- function(vcf.obj)
+ {
      temp.vrange <- as(vcf.obj, "VRanges")</pre>
+
      ret.dta <- cbind(
                           seqnames=as.character(seqnames(temp.vrange)),
                           as.data.frame(ranges(temp.vrange))[,c("start", "end")],
                           ref=ref(temp.vrange),
                           alt=alt(temp.vrange),
                           sample=as.character(sampleNames(temp.vrange)),
                           allele_count=sapply(strsplit(temp.vrange$GT, "\\/"),
                                   function(x) sum(as.integer(x), na.rm=T)),
                           stringsAsFactors=F
                           )
      return(ret.dta[ret.dta$allele_count > 0,])
> geno.all.sc <- makeSchemaFromFunction(populate.samp.alt.table, "sample_alleles", vcf.obj=vcf[1:5])
> vcf.sc <- poplite::append(vcf.sc, geno.all.sc)</pre>
```

Our relationships can be specified as before. One wrinkle here is that there is a dependence in the table structures that is more complicated than in the 'Sample Tracking Database' section above. The first relationship statement below will create a final 'alleles' table with the primary key of 'reference' and the 'alt'

column. As 'sample_allleles' contains the full column structure of 'alleles' plus the 'sample' and 'allele_count' columns it has to be first joined with reference to retrieve its primary key, then joined with the new 'alleles' table to get 'alleles' primary key with the final table resembling: 'alt_ind', 'sample' and 'allele_count'. Just as '.' on the left hand side indicates the primary key of the 'from' table the '.reference' variable indicates the primary key of the reference table.

```
> relationship(vcf.sc, from="reference", to="alleles") <- .~seqnames+start+end+ref
> relationship(vcf.sc, from="reference", to="sample_alleles") <- .~seqnames+start+end+ref
> relationship(vcf.sc, from="alleles", to="sample_alleles") <- .~.reference+alt
>
```

Now that our schema is complete, we can populate our three tables in the database. In this case, we can populate the entire database with one statement, however for demonstration purposes we will divide the VCF object into several pieces and populate them one at a time to simulate reading from a large file in chunks or iterating over several files. Also note that the 'constraint<-' method is available to provide a mechanism to enforce uniqueness of a subset of columns for a given table which is especially useful if the database is being populated from many files which may have duplicate data.

```
> vcf.db <- Database(vcf.sc, tempfile())</pre>
> populate(vcf.db, vcf.obj=vcf[1:1000])
> populate(vcf.db, vcf.obj=vcf[1001:2000])
> pop.res <- as.data.frame(poplite::select(vcf.db, .tables=tables(vcf.db)))
> vrange.tab <- as(vcf[1:2000], "VRanges")</pre>
> vrange.dta <- data.frame(seqnames=as.character(seqnames(vrange.tab)),</pre>
                            start=start(vrange.tab),
                            end=end(vrange.tab),
                            ref=as.character(ref(vrange.tab)),
                            alt=as.character(alt(vrange.tab)),
                            sample=as.character(sampleNames(vrange.tab)),
                            allele_count=sapply(strsplit(vrange.tab$GT, "\\/"),
                                   function(x) sum(as.integer(x), na.rm=T)),
                            stringsAsFactors=F)
> vrange.dta <- vrange.dta[vrange.dta$allele_count > 0,]
> vrange.dta <- vrange.dta[do.call("order", vrange.dta),]</pre>
> sub.pop.res <- pop.res[,names(vrange.dta)]</pre>
> sub.pop.res <- sub.pop.res[do.call("order", sub.pop.res),]</pre>
> all.equal(sub.pop.res, vrange.dta, check.attributes=F)
[1] TRUE
> sessionInfo()
R version 3.4.1 (2017-06-30)
Platform: x86_64-apple-darwin15.6.0 (64-bit)
Running under: OS X El Capitan 10.11.6
Matrix products: default
BLAS: /Library/Frameworks/R.framework/Versions/3.4/Resources/lib/libRblas.0.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/3.4/Resources/lib/libRlapack.dylib
locale:
[1] C/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
attached base packages:
[1] stats4
              parallel stats
                                   graphics grDevices utils
                                                                  datasets
```

[8] methods base

other attached packages:

[1] VariantAnnotation_1.22.3 Rsamtools_1.28.0 [3] Biostrings_2.44.2 XVector_0.16.0 [5] SummarizedExperiment_1.6.4 DelayedArray_0.2.7 [7] matrixStats_0.52.2 Biobase_2.36.2 [9] GenomicRanges_1.28.5 GenomeInfoDb_1.12.2 [11] IRanges_2.10.3 S4Vectors_0.14.4 [13] BiocGenerics_0.22.0 RSQLite_2.0 [15] poplite_0.99.19 DBI_0.7 [17] dplyr_0.7.3

loaded via a namespace (and not attached):

Todaca via a namespace (and not attached):			
[1]	Rcpp_0.12.12	compiler_3.4.1	dbplyr_1.1.0
[4]	bindr_0.1	<pre>GenomicFeatures_1.28.5</pre>	bitops_1.0-6
[7]	tools_3.4.1	zlibbioc_1.22.0	biomaRt_2.32.1
[10]	digest_0.6.12	bit_1.1-12	BSgenome_1.44.1
[13]	lattice_0.20-35	memoise_1.1.0	tibble_1.3.4
[16]	pkgconfig_2.0.1	rlang_0.1.2	Matrix_1.2-11
[19]	igraph_1.1.2	bindrcpp_0.2	<pre>GenomeInfoDbData_0.99.0</pre>
[22]	rtracklayer_1.36.4	bit64_0.9-7	grid_3.4.1
[25]	glue_1.1.1	R6_2.2.2	AnnotationDbi_1.38.2
[28]	XML_3.98-1.9	BiocParallel_1.10.1	blob_1.1.0
[31]	magrittr_1.5	<pre>GenomicAlignments_1.12.2</pre>	assertthat_0.2.0
[34]	RCurl_1.95-4.8	lazyeval_0.2.0	

References

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Valerie Obenchain, Michael Lawrence, Vincent Carey, Stephanie Gogarten, Paul Shannon, and Martin Morgan. Variantannotation: a bioconductor package for exploration and annotation of genetic variants. *Bioinformatics*, 30(14):2076-2078, 2014. doi: 10.1093/bioinformatics/btu168. URL http://bioinformatics.oxfordjournals.org/content/30/14/2076.abstract.

Hadley Wickham and Romain Francois. dplyr: A Grammar of Data Manipulation, 2014. URL http://CRAN.R-project.org/package=dplyr. R package version 0.3.0.2.