

# geuvStore2: sharded storage for cis-association statistics

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# 1 Introduction

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The *geuvStore2* package demonstrates an approach to management of large numbers of statistics generated in integrative genomic analyses. The specific use case demonstrated here is cis-eQTL discovery. The following considerations motivated the design used here.

- Cluster computing will typically be used to perform cis-eQTL searches. Scalable performance is greatly aided by the *BatchJobs* infrastructure, which will create an archive of results.
  - This archive includes a database that holds information on job status (including time and memory required to complete) and result location. We consider this information worth saving.
  - The collection of results is, by default, “sharded” into a reasonable number of folders holding serialized R objects. We find this approach useful for supporting parallelizable retrieval of results.
- It makes sense to store results of cis-association analyses so that queries based on genomic addresses are rapidly resolved. Thus all the results are stored in *GRanges* instances, and queries based on *GRanges* are efficiently resolvable if an optional index is prepared before use.

## 2 Illustration

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### 2.1 Construction of mediator and indices

The most basic entity mediating access to the information is the *BatchJobs* registry object. This is typically not created in a portable format, but includes directory information that we modify during package installation.

```
suppressPackageStartupMessages(library(geuvStore2))
prst = makeGeuvStore2()
prst
## ciseStore instance with 160 completed jobs.
## excerpt from job 1 :
## GRanges object with 1 range and 14 metadata columns:
##      seqnames      ranges strand |      paramRangeID      REF
##      <Rle> <IRanges> <Rle> |      <factor> <DNAStringSet>
## [1]      1      526736      * | ENSG00000215915.5      C
##      ALT      chisq permScore_1 permScore_2 permScore_3 permScore_4
##      <CharacterList> <numeric> <numeric> <numeric> <numeric> <numeric>
## [1]      G      2.46383      3.14567      0.409225      0.157174      0.0298147
##      permScore_5 permScore_6      snp      MAF      probeid      mindist
##      <numeric> <numeric> <character> <numeric>      <character> <numeric>
## [1]      0.164809      0.0123114      rs28863004      0.0910112      ENSG00000215915.5      858333
## -----
## seqinfo: 86 sequences from hg19 genome
```

## geuvStore2: sharded storage for cis-association statistics

Association statistics were recorded between expression levels of each gene (as recorded in the GEUVADIS FPKM report) and all SNP with MAF  $> 10^{-6}$  lying within a radius of 1 million bp upstream or downstream from the gene region. This package provides access to a selection of 160 jobs.

We use the `ciseStore` class to mediate between the user and the results data. This includes optional mappings based on gene identifiers (in the case of this example, these are Ensembl gene IDs) and `GRanges`. We have stored the maps, but they can be computed in real time if need be.

```
library(gQTLBase)
# prstore = ciseStore(prst, addProbeMap=TRUE, addRangeMap=TRUE)
prstore = makeGeuvStore2()
prstore
## ciseStore instance with 160 completed jobs.
## excerpt from job 1 :
## GRanges object with 1 range and 14 metadata columns:
##      seqnames      ranges strand |      paramRangeID      REF
##      <Rle> <IRanges> <Rle> |      <factor> <DNAStrngSet>
## [1]      1      526736      * | ENSG00000215915.5      C
##      ALT      chisq permScore_1 permScore_2 permScore_3 permScore_4
##      <CharacterList> <numeric> <numeric> <numeric> <numeric> <numeric>
## [1]      G      2.46383      3.14567      0.409225      0.157174      0.0298147
##      permScore_5 permScore_6      snp      MAF      probeid      mindist
##      <numeric> <numeric> <character> <numeric> <character> <numeric>
## [1]      0.164809      0.0123114      rs28863004      0.0910112      ENSG00000215915.5      858333
## -----
##      seqinfo: 86 sequences from hg19 genome
```

## 2.2 Extraction of content

For a vector of gene identifiers, all available results are extracted.

```
head(
  extractByProbes(prstore,
    probeids=c("ENSG00000183814.10", "ENSG00000174827.9"))
)
## Warning: executing %dopar% sequentially: no parallel backend registered
## GRanges object with 6 ranges and 15 metadata columns:
##      seqnames      ranges strand |      paramRangeID      REF
##      <Rle> <IRanges> <Rle> |      <factor> <DNAStrngSet>
## [1]      1      225418903      * | ENSG00000183814.10      G
## [2]      1      225419456      * | ENSG00000183814.10      T
## [3]      1      225419667      * | ENSG00000183814.10      G
## [4]      1      225419982      * | ENSG00000183814.10      T
## [5]      1      225420024      * | ENSG00000183814.10      G
## [6]      1      225420751      * | ENSG00000183814.10      C
##      ALT      chisq permScore_1 permScore_2 permScore_3
##      <CharacterList> <numeric> <numeric> <numeric> <numeric>
## [1]      A      0.32568323      0.01610581      1.401192      0.128682
## [2]      C      0.00884050      0.07770474      0.550388      1.676589
```

## geuvStore2: sharded storage for cis-association statistics

```
## [3] C 0.05935801 0.13640765 1.354594 4.647168
## [4] C 1.17690014 0.00242561 4.281534 3.892796
## [5] A 0.00101262 1.24509171 0.789927 3.616449
## [6] T 0.06643631 2.19846779 0.279558 2.548228
## permScore_4 permScore_5 permScore_6 snp MAF
## <numeric> <numeric> <numeric> <character> <numeric>
## [1] 0.919730 5.55960780 4.885144 rs114086886 0.0303371
## [2] 2.213819 2.52197917 2.058412 rs664855 0.2876404
## [3] 1.341423 0.21491332 0.766618 rs665776 0.1730337
## [4] 2.712557 0.00491448 1.373410 rs200681083 0.1101124
## [5] 2.186420 0.00269013 0.308526 rs74968234 0.0573034
## [6] 0.188943 1.29585322 1.205943 rs785167 0.1101124
## probeid mindist jobid
## <character> <numeric> <integer>
## [1] ENSG00000183814.10 999947 20
## [2] ENSG00000183814.10 999394 20
## [3] ENSG00000183814.10 999183 20
## [4] ENSG00000183814.10 998868 20
## [5] ENSG00000183814.10 998826 20
## [6] ENSG00000183814.10 998099 20
## -----
## seqinfo: 86 sequences from hg19 genome
```

For a request based on genomic coordinates, a `GRanges` can be used to query. `findOverlaps` is used, and all results for genes whose regions overlap the query ranges are returned.

```
head(
  extractByRanges(prstore, GRanges("1", IRanges(146000000, width=1e6)))
)
## GRanges object with 6 ranges and 15 metadata columns:
## seqnames ranges strand | paramRangeID REF
## <Rle> <IRanges> <Rle> | <factor> <DNAStrngSet>
## [1] 1 146003411 * | ENSG00000174827.9 A
## [2] 1 146003444 * | ENSG00000174827.9 C
## [3] 1 146003808 * | ENSG00000174827.9 G
## [4] 1 146016381 * | ENSG00000174827.9 G
## [5] 1 146016890 * | ENSG00000174827.9 T
## [6] 1 146019838 * | ENSG00000174827.9 T
## ALT chisq permScore_1 permScore_2 permScore_3
## <CharacterList> <numeric> <numeric> <numeric> <numeric>
## [1] G 0.00535325 8.00434e-02 0.0381542 3.63108e-02
## [2] T 0.75645099 3.23116e-01 1.3235147 1.37257e-01
## [3] A 0.02954061 2.62139e-01 0.0274908 2.74685e-05
## [4] A 0.00492719 3.71660e-06 0.4795752 3.72732e-01
## [5] C 0.55698992 4.86687e-02 0.3847998 5.59305e-01
## [6] C 0.12541108 6.37080e-01 0.3140928 1.48692e+00
## permScore_4 permScore_5 permScore_6 snp MAF
## <numeric> <numeric> <numeric> <character> <numeric>
## [1] 0.21059082 3.997329635 0.236039375 rs150635557 0.02359551
## [2] 0.33684968 0.930174555 1.112522594 rs79556380 0.01685393
## [3] 0.04150629 0.007360637 0.000123050 rs587693118 0.01235955
```

## geuvStore2: sharded storage for cis-association statistics

```
## [4] 0.44955126 0.961466289 0.000589195 rs376735389 0.00449438
## [5] 0.00165828 1.069335374 0.000743055 rs199499386 0.48651685
## [6] 0.07721023 0.000325715 1.556756923 rs201518173 0.24044944
##           probeid   mindist   jobid
##           <character> <numeric> <integer>
## [1] ENSG00000174827.9   239337       6
## [2] ENSG00000174827.9   239370       6
## [3] ENSG00000174827.9   239734       6
## [4] ENSG00000174827.9   252307       6
## [5] ENSG00000174827.9   252816       6
## [6] ENSG00000174827.9   255764       6
## -----
## seqinfo: 86 sequences from hg19 genome
```

## 2.3 Applicative programming

The `storeApply` function will be evaluated on all store elements. Iteration is governed by the `foreach` package.

```
lens = storeApply(prstore, length)
summary(unlist(lens))
##   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 19852  32987   37346   38645  42701 131671
```

## 2.4 Visualization support

As of March 5, 2015 “`biocLite('vcitn/gQTLbrowser')`” will acquire a package including an interactive visualization function. “`example('gQTLbrowser')`” will load a queryable interface into the browser, with tooltips on the Manhattan plot for the selected gene.

## 2.5 Origins

The code used to generate the store follows. The definition of `kpp` actually used is commented out; `data(kpp)` with the installed package will provide the required vector of gene identifiers. is supplied.

```
library(geuvPack)
data(geuFPKM)
seqlevelsStyle(geuFPKM) = "NCBI"
library(GenomeInfoDb)
ok = which(seqnames(geuFPKM) %in% c(1:22, "X"))
geuFPKM = geuFPKM[ok,]

library(gQTLBase)
#load("../INTERACTIVE/geuvExtractStore.rda")
#kpp = geuvExtractStore@probemap[,1]
data("kpp", package="geuvStore2")
```

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```
geuFPKM = geuFPKM[kpp,]

library(gQTLBase)
featlist = balancedFeatList( geuFPKM[order(rowRanges(geuFPKM)),], max=6 )
lens = sapply(featlist,length)
featlist = featlist[ which(lens>0) ]

library(BatchJobs)
regExtrP6 = makeRegistry("extractP6pop", # tile/cis
  packages=c("GenomicRanges", "gQTLstats", "geuvPack",
    "Rsamtools", "VariantAnnotation"), seed=1234)
myf = function(i) {
  if (!exists("geuFPKM")) data(geuFPKM)
  seqlevelsStyle(geuFPKM) = "NCBI"
  curse = geuFPKM[i,]
  load("gsvs.rda")
  svmat = gsvs$sv
  colnames(svmat) = paste0("SV", 1:ncol(svmat))
  colData(curse) = cbind(colData(curse), DataFrame(svmat))
  fmla = as.formula(paste("~popcode+", paste0(colnames(svmat), collapse="+")))
  curse = regressOut(curse, fmla)
  pn = gtpath( paste0("chr", as.character(seqnames(curse)[1])) )
  tf = TabixFile(pn)
  cisAssoc( curse, tf, cisradius=1000000, nperm=6 )
}
batchMap(regExtrP6, myf, featlist )
submitJobs(regExtrP6, job.delay = function(n,i) runif(1,1,3))
```