

# Overview of GGtools for expression genetics

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## 1 Introduction

The *GGtools* package contains infrastructure and demonstration data for joint analysis of transcriptome and genome through combination of DNA expression microarray and high-density SNP genotyping data. For Bioconductor 2.2 we adopted a representation of genotypes due to Clayton (in package *snpMatrix*) allowing reasonably convenient storage and manipulation of 4 megaSNP phase II HapMap genotypes on all the CEPH CEU samples. This contrasts with the previous version of *GGtools* which was limited to 550 kiloSNP and 58 CEU founders.

To give an immediate taste of the capabilities, we attach the package and load some test data.

```
> library(GGtools)
> data(hmceuB36.2021)
> hmceuB36.2021
```

```
snp.matrix-based genotype set:
number of samples: 90
number of chromosomes present: 2
annotation: illuminaHumanv1.db
Expression data dims: 47293 x 90
Phenodata: An object of class "AnnotatedDataFrame"
 sampleNames: NA06985, NA06991, ..., NA12892 (90 total)
varLabels and varMetadata description:
 famid: hapmap family id
 persid: hapmap person id
 ...: ...
 male: logical TRUE if male
 (7 total)
```

Expression data are recoverable in a familiar way:

```
> exprs(hmceuB36.2021)[1:5, 1:5]
```

|               | NA06985   | NA06991   | NA06993   | NA06994   | NA07000   |
|---------------|-----------|-----------|-----------|-----------|-----------|
| GI_10047089-S | 5.983962  | 5.939529  | 5.912270  | 5.891347  | 5.906675  |
| GI_10047091-S | 6.544493  | 6.286516  | 6.244446  | 6.277397  | 6.330893  |
| GI_10047093-S | 9.905235  | 10.353804 | 10.380972 | 9.889223  | 10.155686 |
| GI_10047099-S | 7.993935  | 7.593970  | 8.261215  | 6.598430  | 6.728085  |
| GI_10047103-S | 11.882265 | 12.204753 | 12.249708 | 11.798415 | 12.015252 |

Genotype data have more complex representation.

```
> smList(hmceuB36.2021)
```

```
$`20`
```

```
A snp.matrix with 90 rows and 119921 columns
```

```
Row names: NA06985 ... NA12892
```

```
Col names: rs4814683 ... rs6090120
```

```
$`21`
```

```
A snp.matrix with 90 rows and 50165 columns
```

```
Row names: NA06985 ... NA12892
```

```
Col names: rs885550 ... rs10483083
```

```
> class(smList(hmceuB36.2021)[["20"]])
```

```
[1] "snp.matrix"
```

This shows that we use a named list to hold items of the *snp.matrix* class from *snpMatrix*.

It will generally be unnecessary to probe to this level, but it is instructive to check the underlying representation:

```
> schunk = smList(hmceuB36.2021)[["20"]]
```

```
> schunk@.Data[1:4, 1:4]
```

|         | rs4814683 | rs6076506 | rs6139074 | rs1418258 |
|---------|-----------|-----------|-----------|-----------|
| NA06985 | 03        | 03        | 03        | 03        |
| NA06991 | 02        | 03        | 02        | 02        |
| NA06993 | 01        | 03        | 01        | 01        |
| NA06994 | 01        | 03        | 01        | 01        |

The leading zeroes show that a raw byte representation is used. We can convert to allele codes as follows:

```
> as(schunk[1:4, 1:4], "character")
```

|         | rs4814683 | rs6076506 | rs6139074 | rs1418258 |
|---------|-----------|-----------|-----------|-----------|
| NA06985 | "B/B"     | "B/B"     | "B/B"     | "B/B"     |
| NA06991 | "A/B"     | "B/B"     | "A/B"     | "A/B"     |
| NA06993 | "A/A"     | "B/B"     | "A/A"     | "A/A"     |
| NA06994 | "A/A"     | "B/B"     | "A/A"     | "A/A"     |

The primary method of interest is the genome-wide association study, here applied with expression as the phenotype. Here we execute a founders-only analysis, adjusting for gender, confining attention to chromosome 20:

```
> pd = pData(hmceuB36.2021)
> hmFou = hmceuB36.2021[, which(pd$mothid == 0 & pd$fathid == 0)]
> f1 = gwSnpTests(genesym("CPNE1") ~ male, hmFou, chrnum(20))
```

## 2 Conversion to nucleotide codes

This is currently somewhat cumbersome. Suppose we want to know the specific nucleotide assignments for a given genotype call. For example, rs4814683 for subject NA06985.

```
> schunk["NA06985", "rs4814683"]
```

```
Autosomal snp(s):
[1] "B/B"
```

We need to know a) that the A/B tokens map in lexical order to the nucleotides (A will be the alphabetically first nucleotide for the diallelic call).

Using the `SNPlocs.Hsapiens.dbSNP.20071016` package, we can get the nucleotides:

```
> library(SNPlocs.Hsapiens.dbSNP.20071016)
> s20 = getSNPlocs("chr20")
> s20[s20[, 1] == 4814683, ]
```

```
RefSNP_id alleles_as_ambig loc
4 4814683 K 9795
```

Now we need to translate the IUPAC code to the nucleotides:

```
> library(Biostrings)
> IUPAC_CODE_MAP
```

|       |       |       |        |      |      |      |      |      |      |       |
|-------|-------|-------|--------|------|------|------|------|------|------|-------|
| A     | C     | G     | T      | M    | R    | W    | S    | Y    | K    | V     |
| "A"   | "C"   | "G"   | "T"    | "AC" | "AG" | "AT" | "CG" | "CT" | "GT" | "ACG" |
| H     | D     | B     | N      |      |      |      |      |      |      |       |
| "ACT" | "AGT" | "CGT" | "ACGT" |      |      |      |      |      |      |       |