Bioconductor snpStats Bugs

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1 Introduction

In the Regression and Migration vignette, we discovered that there has been a bug in snpMatrix's single.snp.tests() for many years, which can affect 1% to 2% of SNPs, and fixed it. This vignette uses the testsuite code in snpMatrix to reveal snpStats' bug(s). The quick summary is that most (all?) of the statistical tests were broken to various extent arount October 2008 by the imputation-related changes. That is 3 years of flawed publications. David made an effort with 1.3.7+ (20th October 2011) but did not get very far. This document is usually built against current snpStats HEAD as well as 1.3.6 (17th October 2011), the latter because of the number of flawed results in 3 years.

Despite many routines being of the same names but behaving differently (such as the buggy single.snp.tests() in snpStats vs the correct one in snpMatrix) and a warning about routines shadowing each other, it is possible to use either in the same R session even in alternating statements, as long as either are referenced explicitly in each step. This usually consists of prefix'ing with explicit namespace references (e.g. snpMatrix::single.snp.tests() instead of single.snp.tests()) or adding package= within.

```
> library(snpMatrix)
> library(snpStats)
> sessionInfo()
R version 2.15.3 (2013-03-01)
Platform: i686-redhat-linux-gnu (32-bit)
locale:
 [1] LC_CTYPE=en_GB.utf8
                               LC_NUMERIC=C
 [3] LC_TIME=en_GB.utf8
                               LC_COLLATE=en_GB.utf8
                               LC_MESSAGES=en_GB.utf8
 [5] LC_MONETARY=en_GB.utf8
 [7] LC_PAPER=C
                               LC_NAME=C
 [9] LC_ADDRESS=C
                               LC_TELEPHONE=C
[11] LC_MEASUREMENT=en_GB.utf8 LC_IDENTIFICATION=C
attached base packages:
[1] grDevices datasets splines
                                  graphics utils
                                                       stats
                                                                 methods
[8] base
other attached packages:
[1] snpStats_1.9.3
                        snpMatrix_1.19.0.17 Matrix_1.0-11
[4] lattice_0.20-13
                        survival_2.37-2
loaded via a namespace (and not attached):
```

At this point there is a warning:

[1] BiocGenerics_0.4.0 grid_2.15.3

```
Attaching package: 'snpStats'

The following object(s) are masked from 'package:snpMatrix':

can.impute, chi.squared, col.summary, deg.freedom, effect.sign, effective.sample.size, filter.rules, Fst, glm.test.control, ibsCount, ibsDist, imputation.maf, imputation.nsnp, imputation.r2, impute.snps, ld, misinherits, mvtests, p.value, plotUncertainty, pool, pool2, pp, qq.chisq, read.beagle, read.impute, read.mach, read.pedfile, read.plink, read.snps.long, row.summary, sample.size, single.snp.tests, snp.cbind, snp.cor, snp.imputation,
```

tools_2.15.3

```
snp.lhs.estimates, snp.lhs.tests, snp.post.multiply,
snp.pre.multiply, snp.rbind, snp.rhs.estimates, snp.rhs.tests,
switch.alleles, tdt.snp, test.allele.switch, write.plink, xxt
```

Loading snpMatrix124 simultaneously can also cause a few warnings of the form, understandably:

```
A specification for class MX.snp.matrix in package 'snpMatrix124' seems equivalent to one from package 'snpMatrix' and is not turning on duplicate class definitions for this class
```

The warning is harmless, if one pays attention to specifying each explicitly, as below.

2 Bugs in snpStats GLM estimates

2.1 snpStats::snp.*hs.estimates() returns garbage

snp.*hs.estimates() gives garbage — the way to illustrate this is simply running the corresponding snp.rhs.tests and compare:

```
> data(testdata, package = "snpStats")
> test2 <- snpStats::snp.rhs.estimates(cc ~ region + sex, family = "binomial",
     data = subject.data, snp.data = Autosomes, sets = 1:10)
> test2.t <- snpStats::snp.rhs.tests(cc ~ region + sex, family = "binomial",
     data = subject.data, snp.data = Autosomes, tests = 1:10)
> print(cbind(as(as(test2, "GlmTests"), "data.frame"), as(test2.t,
      "data.frame")))
       Chi.squared Df
                        p.value Chi.squared Df
                                                  p.value
173760 0.002022755 1 0.96412719 0.96172092 1 0.32675367
173761 1.614689875 1 0.20383380 1.61954459 1 0.20315530
173762 2.052781924 1 0.15192836 2.05991420 1 0.15121869
173767 0.777421401 1 0.37793093 0.77858708 1 0.37757361
173769 2.762354385 1 0.09650612 2.92552940 1 0.08718862
173770
               NA NA
                             NA
                                         NA O
                                                       NA
173772 0.002046886 1 0.96391400 1.02511037 1 0.31130988
173774 0.729732211 1 0.39297000 0.73179195 1 0.39230296
173775 0.952718263 1 0.32902835 0.95584241 1 0.32823661
173776 0.090165195 1 0.76396725 0.09019184 1 0.76393342
```

This is the correct result from snpMatrix (1.17.7.11) (Wald test close to the score test):

```
> Autosomes <- new("snp.matrix", Autosomes@.Data)
> test2 <- snpMatrix::snp.rhs.estimates(cc ~ region + sex, family = "binomial",</pre>
```

```
data = subject.data, snp.data = Autosomes, sets = 1:10)
> test2.t <- snpMatrix::snp.rhs.tests(cc ~ region + sex, family = "binomial",
      data = subject.data, snp.data = Autosomes, tests = 1:10)
> print(cbind(as(as(test2, "snp.tests.glm"), "data.frame"), as(test2.t,
      "data.frame")))
       Chi.squared Df
                         p.value Chi.squared Df
                                                   p.value
173760 0.68794335 1 0.40686481 0.96171330 1 0.32675559
                   1 0.20376957 1.61953853 1 0.20315614
173761 1.61514861
173762 2.05337857 1 0.15186885 2.05990584 1 0.15121951
173767 0.77747875 1 0.37791334 0.77858708 1 0.37757361
173769 2.76587572 1 0.09629398 2.92549240 1 0.08719062
173770
                NA NA
                              NA
                                          NA O
                                                        NA
173772 0.71127227 1 0.39902177
                                  1.02511036 1 0.31130988
173774 0.72973283 1 0.39296980
                                 0.73179195 1 0.39230296
173775 0.95271902 1 0.32902816 0.95584109 1 0.32823694
173776 0.09016525 1 0.76396718 0.09019184 1 0.76393341
  See another garbage result from snpStats:
> data(testdata, package = "snpStats")
> test3 <- snpStats::snp.lhs.estimates(Autosomes[, 1:10], ~strata(cc),</pre>
      "strata(region), data = subject.data, robust = TRUE)
> test3.t <- snpStats::snp.lhs.tests(Autosomes[, 1:10], ~strata(cc),</pre>
      "strata(region), data = subject.data, robust = TRUE)
> print(cbind(as(as(test3, "GlmTests"), "data.frame"), as(test3.t,
      "data.frame")))
       Chi.squared Df p.value Chi.squared Df
                                                p.value
                NA NA
173760
                           NA
                                      NaN 0
                                                    NaN
173761
                NA NA
                           NΑ
                                10.263701 9 0.32956204
173762
                NA NA
                           NA
                                10.476287 9 0.31331934
                NA NA
                           NA
                                15.045105 9 0.08970445
173767
173769
                NA NA
                           NA
                                16.267175 9 0.06150760
                                 0.000000 0 1.00000000
173770
                NA NA
                           NA
173772
                NA NA
                           NA
                                      NaN 0
173774
                NA NA
                           NA
                                 9.411857 9 0.40015665
173775
                NA NA
                           NA
                                13.440413 9 0.14366942
                                16.797680 9 0.05198017
173776
                NA NA
                           NA
```

At the time of this writing, snpMatrix (1.17.7.11, unreleased) isn't correct either, but better:

```
> print(cbind(as(as(test3, "snp.tests.glm"), "data.frame"), as(test3.t,
     "data.frame")))
      Chi.squared Df
                          p.value Chi.squared Df
                                                  p.value
173760 1004.549087
                  9 1.801433e-210
                                    1.009134 9 0.99941616
173761
        10.959622 9
                     2.784868e-01
                                   10.263701 9 0.32956204
173762
        11.155682 9 2.651885e-01
                                   10.476287 9 0.31331934
173767
       17.009456 9 4.856810e-02 15.045105 9 0.08970445
173769 201.767706 9 1.411265e-38 16.267175 9 0.06150760
                               NA 0.000000 0 1.00000000
173770
              NA NA
173772
         5.449466 9 7.935005e-01
                                    1.009439 9 0.99941544
173774 278.130321 9 1.125582e-54
                                    9.411857 9 0.40015665
173775 337.152659 9 3.352980e-67
                                   13.440413 9 0.14366942
173776 426.044143 9 3.773047e-86
                                   16.797680 9 0.05198017
```

3 Multiple snpStats issues of data corruption, memory violations and crashes

There are multiple issues of data corruption, memory violation and crashes in the GLM related code. The best way to demonstrate this is turn on gctorture() and uses the GLM score tests/estimates and see R crash.

4 Bugs in snpStats GLM score tests

4.1 snpStats::snp.lhs.tests(...,robust=TRUE) returns garbage

```
> data(testdata, package = "snpStats")
> snpStats::snp.lhs.tests(Autosomes[, 1:10], ~strata(cc), ~strata(region),
      data = subject.data, robust = TRUE)
       Chi.squared Df
                         p.value
173760
               NaN O
        10.263701 9 0.32956204
173761
173762
        10.476287 9 0.31331934
173767
        15.045105 9 0.08970445
173769
        16.267175 9 0.06150760
          0.000000 0 1.00000000
173770
173772
               NaN 0
173774
         9.411857 9 0.40015665
        13.440413 9 0.14366942
173775
173776
        16.797680 9 0.05198017
```

The correct result should be somewhat close to the non-robust result:

```
> snpStats::snp.lhs.tests(Autosomes[, 1:10], ~strata(cc), ~strata(region),
+ data = subject.data, robust = FALSE)
```

```
Chi.squared Df
                        p.value
173760
               NaN
                   9
                            NaN
173761
         12.272003 9 0.1984058
         12.476151 9 0.1877771
173762
173767
         14.462676 9 0.1067926
          8.589652 9 0.4759812
173769
173770
          0.000000 0 1.0000000
173772
               NaN 9
                            NaN
          6.156140 9 0.7241952
173774
173775
          8.812111 9 0.4547958
173776
          7.602749 9 0.5746207
  Now we convert snpStats classes (mixed-cases without ".") to snpMatrix's (lowercases with "."),
and re-run the the snpMatrix version of snp.lhs.tests():
> snpMatrix::snp.lhs.tests(new("snp.matrix", Autosomes@.Data)[,
      1:10], "strata(cc), "strata(region), data = subject.data,
      robust = TRUE)
       Chi.squared Df
                         p.value
173760
          1.009134 9 0.99941616
173761
         10.263701 9 0.32956204
173762
         10.476287 9 0.31331934
173767
         15.045105 9 0.08970445
         16.267175 9 0.06150760
173769
173770
          0.000000 0 1.00000000
         1.009439 9 0.99941544
173772
          9.411857 9 0.40015665
173774
173775
         13.440413 9 0.14366942
173776
         16.797680 9 0.05198017
  Just to see what snpMatrix does without robust:
> snpMatrix::snp.lhs.tests(new("snp.matrix", Autosomes@.Data)[,
      1:10], "strata(cc), "strata(region), data = subject.data,
      robust = FALSE)
       Chi.squared Df
                        p.value
          5.042974 9 0.8305461
173760
173761
         12.272003 9 0.1984058
173762
         12.476151 9 0.1877771
         14.462676 9 0.1067926
173767
          8.589652 9 0.4759812
173769
          0.000000 0 1.0000000
173770
          7.714940 9 0.5631090
173772
173774
          6.156140 9 0.7241952
173775
          8.812111 9 0.4547958
173776
          7.602749 9 0.5746207
```

This bug also exist in snpMatrix prior to 1.17.5.10 and was introduced with the imputation-related changes around October 2008.

See also how snpMatrix124 does:

```
> snpMatrix124::snp.lhs.tests(new("snp.matrix", Autosomes@.Data)[,
      1:10], "strata(cc), "strata(region), data = subject.data,
      robust = TRUE)
       Chi.squared Df Df.residual
173760
          1.008943 8
173761
         10.263701 9
                              398
173762
        10.476287 9
                              396
173767
        15.045105 9
                              376
173769
        16.006621 8
                              394
173770
                NA NA
                               NA
173772
          1.009439
                    8
                              199
173774
         9.411857 9
                              386
173775
        13.440413 9
                              397
        16.797680 9
173776
                              398
> snpMatrix124::snp.lhs.tests(new("snp.matrix", Autosomes@.Data)[,
      1:10], "strata(cc), "strata(region), data = subject.data,
      robust = FALSE)
       Chi.squared Df Df.residual
          5.042974 9
173760
173761
         12.272003 9
                              398
173762
        12.476151 9
                              396
173767
        14.462676 9
                              376
173769
          8.589652 9
                              394
                NA NA
173770
                               NA
173772
         7.714940 9
                              199
173774
          6.156140 9
                              386
173775
          8.812111
                              397
173776
          7.602749 9
                              398
```

4.2 Malformed "GlmTests" S4 object from snpStats::snp.lhs.tests()

Upto and including snpStats 1.3.6:

```
> result <- snpStats::snp.lhs.tests(Autosomes[, 1:10], ~strata(cc),
+ ~strata(region), data = subject.data)</pre>
```

Looking at result gives a hard error so I'll just show the message below:

```
> str(result)
Error in FUN(c("snp.names", "var.names", "chisq", "df", "N")[[2L]], ...) :
  no slot of name "var.names" for this object of class "GlmTests"
```

There is no need to show the alternatives as this is clearly broken.

This bug is specific to snpStats and has no equivalent in snpMatrix.

4.3 Crazy large/negative number of samples from snpStats GLM tests

Upto and including snpStats 1.3.6:

> result@N

- [1] 202248192 202248160 202248128 202248096 202248064 202248032 202248000
- [8] 202247968 202247936 202247904

Hundred million samples and negative number of samples?

This bug also exist in snpMatrix prior to 1.17.5.10 and was introduced with the imputation-related changes around October 2008.

4.4 snpStats::snp.rhs.tests() returning garbage with or without robust

```
> snpStats::snp.rhs.tests(cc ~ strata(region, sex), family = "binomial",
+ data = subject.data, snp.data = Autosomes, tests = 1:10)
```

```
Chi.squared Df
                         p.value
       1.25356125
173760
                   1 0.26287339
173761
       1.61290542 1 0.20408387
                  1 0.15298186
173762
       2.04226350
173767
               {\tt NaN}
                   1
                             NaN
173769
       3.54351327
                   1 0.05977872
173770
                NA
173772 0.59863946 1 0.43909761
173774 0.82443150 1 0.36388768
173775 0.87744532 1 0.34890234
173776 0.09218633 1 0.76141588
```

The correct result shouldn't be too far from without sex:

```
> snpStats::snp.rhs.tests(cc ~ strata(region), family = "binomial",
+ data = subject.data, snp.data = Autosomes, tests = 1:10)
```

```
Chi.squared Df p.value
173760 1.01538462 1 0.31361630
173761 1.46259571 1 0.22651757
173762 1.92028786 1 0.16582493
173767 0.77609738 1 0.37833736
173769 2.92614948 1 0.08715513
173770 NA 0 NA
173772 1.11008326 1 0.29206385
173774 0.66697270 1 0.41410906
173775 0.96730037 1 0.32535438
173776 0.09831885 1 0.75385649
```

Here is how snpMatrix does it:

```
> snpMatrix::snp.rhs.tests(cc ~ strata(region, sex), family = "binomial",
      data = subject.data, snp.data = new("snp.matrix", Autosomes@.Data),
      tests = 1:10)
       Chi.squared Df
                         p.value
173760 1.25356125 1 0.26287339
173761 1.61290542 1 0.20408387
173762 2.04226350 1 0.15298186
173767 0.29671726 1 0.58594776
173769 3.54351327 1 0.05977872
173770
               NA O
                              NA
173772 0.59863946 1 0.43909761
173774 0.82443150 1 0.36388768
173775 0.87744532 1 0.34890234
173776 0.09218633 1 0.76141588
  Just to see that snpMatrix does it without sex:
> snpMatrix::snp.rhs.tests(cc ~ strata(region), family = "binomial",
      data = subject.data, snp.data = new("snp.matrix", Autosomes@.Data),
      tests = 1:10)
       Chi.squared Df
                         p.value
173760 1.01538462 1 0.31361630
173761 1.46259571 1 0.22651757
173762 1.92028786 1 0.16582493
173767 0.77609738 1 0.37833736
173769 2.92614948 1 0.08715513
173770
               NA O
173772 1.11008326 1 0.29206385
173774 0.66697270 1 0.41410906
173775 0.96730037
                    1 0.32535438
173776 0.09831885 1 0.75385649
   This bug also exist in snpMatrix prior to 1.17.5.10 and was introduced with the imputation-
related changes around October 2008.
  See how snpMatrix124 does:
> snpMatrix124::snp.rhs.tests(cc ~ strata(region, sex), family = "binomial",
      data = subject.data, snp.data = new("snp.matrix", Autosomes@.Data),
      tests = 1:10)
       Chi.squared Df Df.residual
173760 1.25356125 1
                              373
173761 1.61290542 1
                              376
```

```
173762 2.04226350 1
                              374
173767 0.29671726 1
                              350
173769 3.54958407 1
                              372
173770
                NA NA
                              376
173772 0.59863946 1
                              376
173774 0.82443150 1
                              365
173775 0.87744532 1
                              375
173776 0.09218633 1
                              376
> snpMatrix124::snp.rhs.tests(cc ~ strata(region), family = "binomial",
      data = subject.data, snp.data = new("snp.matrix", Autosomes@.Data),
      tests = 1:10)
       Chi.squared Df Df.residual
173760 1.01538462 1
173761 1.46259571 1
                              390
173762 1.92028786 1
                              388
173767 0.77609738 1
                              368
173769 2.92614948 1
                              386
173770
                              390
               NA NA
173772 1.11008326 1
                              390
173774 0.66697270 1
                              378
173775 0.96730037 1
                              389
173776 0.09831885 1
                              390
    2-df Bug in snpStats::single.snp.tests()
5
> data(for.exercise, package = "snpStats")
> tests.snpStats <- snpStats::single.snp.tests(cc, stratum, data = subject.support,
      snp.data = snps.10)
  Now we convert snpStats classes (mixed-cases without ".") to snpMatrix's (lowercases with "."),
and re-run the the snpMatrix version of single.snp.tests():
> str(snps.10)
Formal class 'SnpMatrix' [package "snpStats"] with 1 slots
  ..@ .Data: raw [1:1000, 1:28501] 01 01 01 01 ...
  ... - attr(*, "dimnames")=List of 2
  .....$ : chr [1:1000] "jpt.869" "jpt.862" "jpt.948" "ceu.564" ...
  .....$ : chr [1:28501] "rs7909677" "rs7093061" "rs12773042" "rs7475011" ...
> snps.10 <- new("snp.matrix", snps.100.Data)
> str(snps.10)
Formal class 'snp.matrix' [package "snpMatrix"] with 1 slots
  ..@ .Data: raw [1:1000, 1:28501] 01 01 01 01 ...
```

```
... - attr(*, "dimnames")=List of 2
  .....$ : chr [1:1000] "jpt.869" "jpt.862" "jpt.948" "ceu.564" ...
  .....$ : chr [1:28501] "rs7909677" "rs7093061" "rs12773042" "rs7475011" ...
> tests.snpMatrix <- snpMatrix::single.snp.tests(cc, stratum, data = subject.support,
      snp.data = snps.10)
  Then we use the testsuite code to compare:
> all.equal(tests.snpStats@chisq[, "1 df"], tests.snpMatrix@chisq[,
      "1 df"], tolerance = 0)
[1] TRUE
> all.equal(tests.snpStats@chisq[, "2 df"], tests.snpMatrix@chisq[,
      "2 df"], tolerance = 0)
[1] "'is.NA' value mismatch: 789 in current 807 in target"
> snpMatrix:::.chi2.all.equal(tests.snpStats@chisq[, "2 df"], tests.snpMatrix@chisq[,
      "2 df"])
Max absolute finite difference: 0
Max relative finite difference: 0
Finite in 1st but not in 2nd: 0
Finite in 2nd but not in 1st: 18
  Min. 1st Qu. Median Mean 3rd Qu.
                                           Max.
0.8604 1.2830 2.4020 2.3000 2.9840 4.2580
Difference
        18
  Or 20 SNP tests failed in snpStats but okay in snpMatrix.
  Now we run the non-stratified tests, but convert in the opposite direction, and compare:
> tests.snpMatrix.crude <- snpMatrix::single.snp.tests(cc, data = subject.support,
      snp.data = snps.10)
> str(snps.10)
Formal class 'snp.matrix' [package "snpMatrix"] with 1 slots
  ..@ .Data: raw [1:1000, 1:28501] 01 01 01 01 ...
  ... - attr(*, "dimnames")=List of 2
  .....$ : chr [1:1000] "jpt.869" "jpt.862" "jpt.948" "ceu.564" ...
  .....$ : chr [1:28501] "rs7909677" "rs7093061" "rs12773042" "rs7475011" ...
> snps.10 <- new("SnpMatrix", snps.10@.Data)
> str(snps.10)
```

```
Formal class 'SnpMatrix' [package "snpStats"] with 1 slots
  ..@ .Data: raw [1:1000, 1:28501] 01 01 01 01 ...
  ... - attr(*, "dimnames")=List of 2
  .....$: chr [1:1000] "jpt.869" "jpt.862" "jpt.948" "ceu.564" ...
  .....$ : chr [1:28501] "rs7909677" "rs7093061" "rs12773042" "rs7475011" ...
> tests.snpStats.crude <- snpStats::single.snp.tests(cc, data = subject.support,
      snp.data = snps.10)
> all.equal(tests.snpStats.crude@chisq[, "2 df"], tests.snpMatrix.crude@chisq[,
      "2 df"], tolerance = 0)
[1] "'is.NA' value mismatch: 789 in current 807 in target"
> snpMatrix:::.chi2.all.equal(tests.snpStats.crude@chisq[, "2 df"],
      tests.snpMatrix.crude@chisq[, "2 df"])
Max absolute finite difference: 0
Max relative finite difference: 0
Finite in 1st but not in 2nd: 0
Finite in 2nd but not in 1st: 18
  Min. 1st Qu. Median Mean 3rd Qu.
                                          Max.
          1.408 2.405 2.323
  1.043
                                  2.865
                                         3.922
Difference
        18
  Or 18 SNP tests failed in snpStats but okay in snpMatrix.
```

This bug also exist in snpMatrix prior to 1.17.4.9 for its entire history (i.e. since pre-1.0), and differently before 1.5.x also.

This explains why snpStats and snpMatrix124 differs:

```
> snps.10 <- new("snp.matrix", snps.100.Data)</pre>
> tests.snpMatrix124 <- snpMatrix124::single.snp.tests(cc, stratum,</pre>
      data = subject.support, snp.data = snps.10)
> all.equal(tests.snpStats@chisq[, "1 df"], tests.snpMatrix124$chi2.1df,
      tolerance = 0)
[1] "Mean relative difference: 1.790103e-16"
> all.equal(tests.snpStats@chisq[, "2 df"], tests.snpMatrix124$chi2.2df,
      tolerance = 0)
[1] "'is.NA' value mismatch: 789 in current 807 in target"
> snpMatrix:::.chi2.all.equal(tests.snpMatrix124$chi2.1df, tests.snpMatrix@chisq[,
      "1 df"])
```

```
Max absolute finite difference: 7.105427e-15
Max relative finite difference: 8.941748e-13
Finite in 1st but not in 2nd: 0
Finite in 2nd but not in 1st: 0
Difference
> snpMatrix:::.chi2.all.equal(tests.snpStats@chisq[, "2 df"], tests.snpMatrix124$chi2.2df)
Max absolute finite difference: 3.819167e-14
Max relative finite difference: 2.35139e-14
Finite in 1st but not in 2nd: 0
Finite in 2nd but not in 1st: 18
  Min. 1st Qu. Median
                          Mean 3rd Qu.
                                           Max.
 0.8604 1.2830 2.4020 2.3000 2.9840 4.2580
Difference
        18
> snpMatrix:::.chi2.all.equal(tests.snpMatrix124$chi2.2df, tests.snpMatrix@chisq[,
      "2 df"])
Max absolute finite difference: 3.819167e-14
Max relative finite difference: 4.193517e-14
Finite in 1st but not in 2nd: 0
Finite in 2nd but not in 1st: 0
Difference
         0
```

So out of 20 of those SNPs that snpStats failed, snpMatrix124 can do 18 and much closer to $snpMatrix\ 1.17.6.10+$.

6 Inputs/Conversions of uncertain genotypes from posterior probabilities

There is a compiler/optimization-dependent bug in inputs/conversions of uncertain genotypes from posterior probabilities, where basically garbage-in, garbage-out. It is seen on Linux/gcc, and possibly all gcc-based systems at normal usage. This means all common systems, since R on windows also uses gcc.

It is fixed in snpMatrix 1.19.0.14 onwards (although snpMatrix does not use uncertain genotypes anywhere up to and including 1.19.0.14), and in snpStats x.x.x.2, 1.7.3.2 being the lowest version with the fix.

7 cbind/rbind in snpStats 1.7.4 onwards

cbind/rbind in snpStats 1.7.4 was rewritten. It does not work under some of the normal use-cases.

Incidentally, it was me who wrote the relevant part of R's cbind/rbind¹ in January 2006, as well as sub-assignments² of RAW types.

8 ld() is broken, has always been broken

The 1d() function introduced in snpStats 1.1.8 (2011-02-15) is broken, and has always been broken. This was first discovered with snpStats 1.9.0<->1.9.1 which changes it slightly. Before or after the change, some snps with non-zero call rates could have NA for r^2 . (r^2 at worst is zero for uncorrelated but called snps). Wrong answers affect up to 5% of SNP pairs in typical datasets (e.g. hapmap).

The older ld.snps() function in snpMatrix is not affected. It was tested against haploview in 2006. As a result, haploview gained an enhancement in this area — for easier comparison! (Sun Apr 23 13:19:26 2006, "cache and show last popup" — the forwarded patch was committed by Jeff), and I gained commit rights to HaploView's repository and tagged HTL_POST_SERIALVER_CHANGE, HTL_PRE_SERIALVER_CHANGE, committed a major clean-up which touched almost half of the files (49 out of 102, to be precise) (Mon Feb 11 19:21:34 2008, "Talked to Jeff Barrett a while ago about this...", committed myself) of HaploView. See Haploview's CVS commit logs for details.

9 64-bit mode for snpStats::single.snp.tests()

This returns all zeros in 64-bit machine occasionally (corruption?):

```
snp.lhs.tests(Autosomes[,1:10], ~cc, ~region, data=subject.data)
```

10 X chromosome conversion

The corresponding X-chromosome conversion is as follows:

```
> data(testdata, package = "snpStats")
> str(Xchromosome)

Formal class 'XSnpMatrix' [package "snpStats"] with 2 slots
    ..@ .Data : raw [1:400, 1:155] 03 03 03 01 ...
    ... - attr(*, "dimnames")=List of 2
    ... ..$ : chr [1:400] "1987" "436" "762" "1199" ...
    ... ..$ : chr [1:155] "174193" "174196" "174197" "174208" ...
    ... @ diploid: Named logi [1:400] TRUE FALSE TRUE FALSE FALSE FALSE ...
    ... - attr(*, "names")= chr [1:400] "1987" "436" "762" "1199" ...
> Xchromosome <- new("X.snp.matrix", Xchromosome@.Data, Female = Xchromosome@diploid)
> str(Xchromosome)
```

Bug 8529 - rbind/cbind unimplemented for raw (RAWSXP) types. https://bugs.r-project.org/bugzilla3/show_bug.cgi?id=8529

²Bug 8530 - sub* assgnment unimplemented for raw (RAWSXP) types. https://bugs.r-project.org/bugzilla3/show_bug.cgi?id=8530

```
Formal class 'X.snp.matrix' [package "snpMatrix"] with 2 slots
..@ .Data : raw [1:400, 1:155] 03 03 03 01 ...
...- attr(*, "dimnames")=List of 2
.....$ : chr [1:400] "1987" "436" "762" "1199" ...
....$ : chr [1:155] "174193" "174196" "174197" "174208" ...
..@ Female: Named logi [1:400] TRUE FALSE TRUE FALSE FALSE FALSE ...
...- attr(*, "names")= chr [1:400] "1987" "436" "762" "1199" ...
```