

The R package *trioClasses* for definition of the class *SNPTrioExperiment*, an extension of *SummarizedExperiment*, for use in trio based analyses of genetic data.

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1 Packages

```
> library("trioClasses")
```

2 Sample Data

```
> data("sample")
> se <- SummarizedExperiment(assays = SimpleList(geno = t(sm)),
  colData = col.DF, rowData = gr)
```

2.1 Pedigree

```
> ped <- PedClass(ped.DF)
```

2.2 SNPTrioExperiment

```
> ste <- SNPTrioExperiment(se, pedigree = ped)
```

```
> ste
```

```
class: SNPTrioExperiment
dim: 511 968
exptData(0):
assays(1): geno
rownames(511): chr14:54383433 chr14:54383470 ...
  chr14:54444385 chr14:54444750
rowData metadata column names(0):
colnames(968): H_ME-CSc175_1-CSc175_1_a.1
  H_ME-CSc175_2-CSc175_2 ... H_ME-DS11418_2-DS11418_2
  H_ME-DS11418_3-DS11418_3
colData names(28): vcfid jb_famid ... id ped
pedigree(4139): famid id fid mid sex dx
```

3 Methods

3.1 ScanTrio

Run ScanTrio for windows of size 1 kB centered at each of the first ten rare variants.

```
> ste.rare <- ste[MAF(ste) <= 0.01]
> (scan.trio <- ScanTrio(object = ste.rare, window = rowData(ste.rare[1:10]) +
  1000/2, block = range(rowData(ste))))
```

	inside	outside
chr14:54383433	2	140
chr14:54383819	2	140
chr14:54384232	2	140
chr14:54384251	2	140
chr14:54384658	4	138
chr14:54384847	4	138
chr14:54384907	4	138
chr14:54384924	4	138
chr14:54384970	4	138
chr14:54385150	4	138

3.2 Holger-style Genotype Matrix

Coercion to matrix for *trio*

```
> geno <- as(ste, "matrix")
> aTDT(geno[, 1:5])
```

\$stat

```
[1] 1.000000 0.000000 0.000000 8.727273 19.565217
```

\$pval

```
[1] 3.173105e-01 1.000000e+00 1.000000e+00 3.134851e-03 9.722321e-06
```

\$transMinor

```
[1] 0 9 2 108 8
```

\$transMajor

```
[1] 1 9 2 156 38
```

Or apply the aTDT method to the SNP TrioExperiment directly.

```
> aTDT(ste[1:5])
```

\$stat

```
[1] 1.000000 0.000000 0.000000 8.727273 19.565217
```

\$pval

```
[1] 3.173105e-01 1.000000e+00 1.000000e+00 3.134851e-03 9.722321e-06
```

\$transMinor

```
[1] 0 9 2 108 8
```

```
$transMajor
```

```
[1] 1 9 2 156 38
```

A Count of Transmission of Variants (*TransCount()*)

A.1 Window

```
> window <- GRanges(seqnames = "chr14", IRanges(start(gr[100]),
  width = 10000), strand = "*")
> window2 <- GRanges(seqnames = "chr14", IRanges(start(gr[100]),
  width = 1000), strand = "*")
> block <- range(rowData(ste))

> TransCount(ste, window)

[1] 1106
```

A.2 Not in window, but in block

```
> TransCount(ste, setdiff(block, window))

[1] 7727
```

A.3 In the whole block

```
> TransCount(ste, block)

[1] 8833
```

A.4 In both windows

```
> TransCount(ste, GRangesList(window, window2))

[1] 1106 48
```

A.5 Not “In both windows,” but in block

```
> TransCount(ste, GRangesList(setdiff(block, window), setdiff(block,
  window2)))

[1] 7727 8785
```

B Count of Transmission of Rare Variants (*TransCount()*)

```
> ste.rare <- ste[MAF(ste) <= 0.01]
```

B.1 In both windows

```
> TransCount(ste.rare, GRangesList(window, window2))

[1] 26 3
```

B.2 Not “In both windows,” but in block

```
> TransCount(ste.rare, GRangesList(setdiff(block, window),
  setdiff(block, window2)))
```

```
[1] 116 139
```

C Classes

C.1 SnpMatrix, DataFrame, GRanges

The four key ingredients are the SNP matrix, the pedigree information as a DataFrame, position of the SNPs given by a GRanges object, and covariate data given as a DataFrame.

```
> sm
```

```
A SnpMatrix with 968 rows and 511 columns
Row names: H_ME-DS10776_2-DS10776_2 ... H_ME-DS11313_1-DS11313_1
Col names: chr14:54383433 ... chr14:54444750
```

```
> ped.DF
```

```
DataFrame with 4139 rows and 6 columns
```

	famid		id
	<character>		<character>
1	4778	H_ME-4778_1-4778_1.2	
2	4778	H_ME-4778_2-4778_2.2	
3	4778	H_ME-4778_3-4778_3.2	
4	4783	H_ME-4783_1-4783_1.1	
5	4783	H_ME-4783_2-4783_2.1	
6	4783	H_ME-4783_3-4783_3.1	
7	20000492	H_ME-20000492_1-20000492_1.1	
8	20000492	H_ME-20000492_2-20000492_2.a.1	
9	20000492	H_ME-20000492_3-20000492_3.1	
...	
4131	DS12332	H_ME-DS12332_1-DS12332_1	
4132	DS12332	H_ME-DS12332_2-DS12332_2	
4133	DS12332	H_ME-DS12332_3-DS12332_3	
4134	DS99998	H_ME-DS10193_5-DS10193_5.2	
4135	DS99998	H_ME-DS10193_6-DS10193_6	
4136	DS99998	H_ME-DS10193_7-DS10193_7	
4137	DS99999	H_ME-DS10707_4-DS10707_4.2	
4138	DS99999	H_ME-DS10707_5-DS10707_5	
4139	DS99999	H_ME-DS10707_6-DS10707_6	
	famid		mid
	<character>		<character>
1	H_ME-4778_2-4778_2.2	H_ME-4778_3-4778_3.2	
2	NA	NA	
3	NA	NA	
4	H_ME-4783_2-4783_2.1	H_ME-4783_3-4783_3.1	
5	NA	NA	

```

6          NA          NA
7  H_ME-20000492_2-20000492_2_a.1 H_ME-20000492_3-20000492_3.1
8          NA          NA
9          NA          NA
...
4131      H_ME-DS12332_2-DS12332_2      H_ME-DS12332_3-DS12332_3
4132          NA          NA
4133          NA          NA
4134      H_ME-DS10193_6-DS10193_6      H_ME-DS10193_7-DS10193_7
4135          NA          NA
4136          NA          NA
4137          NA          NA
4138      H_ME-DS10707_4-DS10707_4.2      H_ME-DS10707_6-DS10707_6
4139          NA          NA

```

```

      sex      dx
<numeric> <numeric>
1          1      1
2          1      0
3          2      0
4          2      1
5          1      0
6          2      1
7          2      1
8          1      0
9          2      0
...
4131      1      1
4132      1      0
4133      2      0
4134      2      1
4135      1      0
4136      2      0
4137      1      0
4138      1      1
4139      2      0

```

```
> gr
```

GRanges with 511 ranges and 0 metadata columns:

```

      seqnames      ranges strand
      <Rle>      <IRanges> <Rle>
chr14:54383433 chr14 [54383433, 54383433] *
chr14:54383470 chr14 [54383470, 54383470] *
chr14:54383819 chr14 [54383819, 54383819] *
chr14:54383945 chr14 [54383945, 54383945] *
chr14:54384030 chr14 [54384030, 54384030] *
chr14:54384232 chr14 [54384232, 54384232] *
chr14:54384251 chr14 [54384251, 54384251] *
chr14:54384291 chr14 [54384291, 54384291] *
chr14:54384382 chr14 [54384382, 54384382] *
...
chr14:54443495 chr14 [54443495, 54443495] *

```

```

chr14:54443499    chr14 [54443499, 54443499]    *
chr14:54443514    chr14 [54443514, 54443514]    *
chr14:54443831    chr14 [54443831, 54443831]    *
chr14:54443880    chr14 [54443880, 54443880]    *
chr14:54444016    chr14 [54444016, 54444016]    *
chr14:54444124    chr14 [54444124, 54444124]    *
chr14:54444385    chr14 [54444385, 54444385]    *
chr14:54444750    chr14 [54444750, 54444750]    *
---
seqlengths:
chr14
NA

```

C.2 SummarizedExperiment

We combine three of the key ingredients when we create the SummarizedExperiment object.

```

> se <- SummarizedExperiment(assays = SimpleList(geno = t(sm)),
  colData = col.DF, rowData = gr)

```

C.3 SNP Trio Experiment

Now, we include the pedigree information as an object of class PedClass. We keep PedClass independent of SNP Trio Experiment for flexibility.

```

> ped <- PedClass(ped.DF)
> ste <- SNP Trio Experiment(se, pedigree = ped)

```

Here is the show method.

```

> ste

class: SNP Trio Experiment
dim: 511 968
exptData(0):
assays(1): geno
rownames(511): chr14:54383433 chr14:54383470 ...
  chr14:54444385 chr14:54444750
rowData metadata column names(0):
colnames(968): H_ME-CSc175_1-CSc175_1_a.1
  H_ME-CSc175_2-CSc175_2 ... H_ME-DS11418_2-DS11418_2
  H_ME-DS11418_3-DS11418_3
colData names(28): vcfid jb_famid ... id ped
pedigree(4139): famid id fid mid sex dx

```

And now we verify that it is indeed an extension of SummarizedExperiment.

```

> getClass("SNP Trio Experiment")

Class "SNP Trio Experiment" [package "trioClasses"]

Slots:

```

```

Name:          pedigree          exptData
Class:         PedClass          SimpleList

Name:          rowData          colData
Class: GenomicRangesORGRangesList DataFrame

Name:          assays
Class:         Assays

Extends: "SummarizedExperiment"

```

C.4 PedClass

Now we investigate the pedigree slot of the SNP Trio Experiment object.

```

> class(pedigree(ste))

[1] "PedClass"
attr(,"package")
[1] "trioClasses"

> getClass("PedClass")

Class "PedClass" [package "trioClasses"]

Slots:

Name:          rownames          nrows          listData
Class: characterORNULL          integer          list

Name:          elementType elementMetadata          metadata
Class:          character DataTableORNULL          list

Extends:
Class "DataFrame", directly
Class "DataTable", by class "DataFrame", distance 2
Class "SimpleList", by class "DataFrame", distance 2
Class "DataTableORNULL", by class "DataFrame", distance 3
Class "List", by class "DataFrame", distance 3
Class "Vector", by class "DataFrame", distance 4
Class "Annotated", by class "DataFrame", distance 5

> pedigree(ste)

PedClass with 4139 rows and 6 columns
      famid          id
    <factor>      <factor>
1      4778      H_ME-4778_1-4778_1.2
2      4778      H_ME-4778_2-4778_2.2
3      4778      H_ME-4778_3-4778_3.2
4      4783      H_ME-4783_1-4783_1.1

```


5	4783	H_ME-4783_2-4783_2.1	
6	4783	H_ME-4783_3-4783_3.1	
7	20000492	H_ME-20000492_1-20000492_1.1	
8	20000492	H_ME-20000492_2-20000492_2_a.1	
9	20000492	H_ME-20000492_3-20000492_3.1	
...	
4131	DS12332	H_ME-DS12332_1-DS12332_1	
4132	DS12332	H_ME-DS12332_2-DS12332_2	
4133	DS12332	H_ME-DS12332_3-DS12332_3	
4134	DS99998	H_ME-DS10193_5-DS10193_5.2	
4135	DS99998	H_ME-DS10193_6-DS10193_6	
4136	DS99998	H_ME-DS10193_7-DS10193_7	
4137	DS99999	H_ME-DS10707_4-DS10707_4.2	
4138	DS99999	H_ME-DS10707_5-DS10707_5	
4139	DS99999	H_ME-DS10707_6-DS10707_6	
		fid	mid
		<factor>	<factor>
1		H_ME-4778_2-4778_2.2	H_ME-4778_3-4778_3.2
2		NA	NA
3		NA	NA
4		H_ME-4783_2-4783_2.1	H_ME-4783_3-4783_3.1
5		NA	NA
6		NA	NA
7		H_ME-20000492_2-20000492_2_a.1	H_ME-20000492_3-20000492_3.1
8		NA	NA
9		NA	NA
...	
4131		H_ME-DS12332_2-DS12332_2	H_ME-DS12332_3-DS12332_3
4132		NA	NA
4133		NA	NA
4134		H_ME-DS10193_6-DS10193_6	H_ME-DS10193_7-DS10193_7
4135		NA	NA
4136		NA	NA
4137		NA	NA
4138		H_ME-DS10707_4-DS10707_4.2	H_ME-DS10707_6-DS10707_6
4139		NA	NA
	sex	dx	
	<factor>	<factor>	
1	1	1	
2	1	0	
3	2	0	
4	2	1	
5	1	0	
6	2	1	
7	2	1	
8	1	0	
9	2	0	
...	
4131	1	1	
4132	1	0	
4133	2	0	

4134	2	1
4135	1	0
4136	2	0
4137	1	0
4138	1	1
4139	2	0

C.5 geno accessor

```
> class(geno(ste))

[1] "SnpMatrix"
attr("package")
[1] "snpStats"

> getClass("SnpMatrix")

Class "SnpMatrix" [package "snpStats"]

Slots:

Name:      .Data
Class: matrix

Extends:
Class "matrix", from data part
Class "array", by class "matrix", distance 2
Class "mMatrix", by class "matrix", distance 2
Class "structure", by class "matrix", distance 3
Class "vector", by class "matrix", distance 4, with explicit coerce

Known Subclasses: "XSnpMatrix"

> geno(ste)

A SnpMatrix with 968 rows and 511 columns
Row names:  H_ME-CSc175_1-CSc175_1_a.1 ... H_ME-DS11418_3-DS11418_3
Col names:  chr14:54383433 ... chr14:54444750
```

C.6 RowData

```
> rowData(ste)

GRanges with 511 ranges and 0 metadata columns:
      seqnames      ranges strand
      <Rle>        <IRanges> <Rle>
chr14:54383433 chr14 [54383433, 54383433] *
chr14:54383470 chr14 [54383470, 54383470] *
chr14:54383819 chr14 [54383819, 54383819] *
chr14:54383945 chr14 [54383945, 54383945] *
chr14:54384030 chr14 [54384030, 54384030] *
```

```

chr14:54384232    chr14 [54384232, 54384232]    *
chr14:54384251    chr14 [54384251, 54384251]    *
chr14:54384291    chr14 [54384291, 54384291]    *
chr14:54384382    chr14 [54384382, 54384382]    *
...
chr14:54443495    chr14 [54443495, 54443495]    *
chr14:54443499    chr14 [54443499, 54443499]    *
chr14:54443514    chr14 [54443514, 54443514]    *
chr14:54443831    chr14 [54443831, 54443831]    *
chr14:54443880    chr14 [54443880, 54443880]    *
chr14:54444016    chr14 [54444016, 54444016]    *
chr14:54444124    chr14 [54444124, 54444124]    *
chr14:54444385    chr14 [54444385, 54444385]    *
chr14:54444750    chr14 [54444750, 54444750]    *
---
seqlengths:
chr14
NA

```

C.7 ColData

D Validity