strum package - examples

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This document contains the whole analysis process for the first three example models from the introduction document. Note that the input data used for these examples are not necessarily simulated to give a meaningful result for each analysis.

```
> library(strum)
```

1 Genetic association analysis

This is an example of a typical genetic association analysis model with a latent trait (similar to MIMIC model). Suppose that there are three measurements (P1, P2 and P3), and it is hypothesized that there is a single latent trait (L1) underlying the three measurements. The latent variable L1 is influenced by a SNP and a set of variance components, polygenic(p) and random environmental(e). Each trait is also influenced by its own random environmental factor. This is the model diagram.

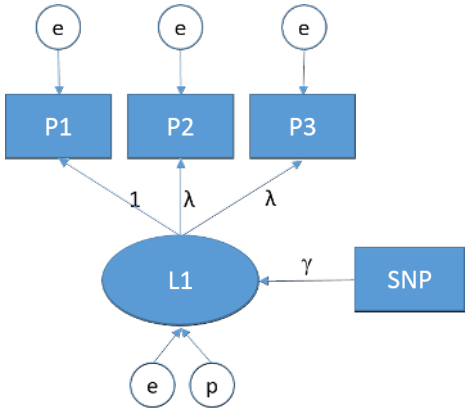

Figure 1: Genetic association analysis model

1.1 Construct model

The first step is to construct a **strumModel** object specifying the above model using *createStrumModel()* function.

```
> assoForm1 =
+   'L1 =~ P1 + P2 + P3 + <e>
+    L1 ~ aSNP + <p,e>
+   '
> myAssoModel = createStrumModel(formulas = assoForm1)

 Creating strumModel ............................. Done

> myAssoModel

Basic properties of the model:
         Model Class ................... strumModel
         Ascertainment ..................... FALSE

List of all variables:
       Obs Covariate InEita   InY Exogen.
L1   FALSE     FALSE   TRUE FALSE   FALSE
aSNP  TRUE      TRUE  FALSE FALSE      NA
P1    TRUE     FALSE  FALSE  TRUE      NA
P2    TRUE     FALSE  FALSE  TRUE      NA
P3    TRUE     FALSE  FALSE  TRUE      NA

Model formulas:
  L1 =~ P1 + P2 + P3 + <e>
  L1 ~ aSNP + <p,e>
```

1.2 Prepare data

The next step is to prepare data. In this example, the data must be a data.frame with 4 required fields - family, id, father, mother, since the model includes the polygenic variance component (p). To run a strum analysis, you need to construct a **strumData** object created by the *createStrumData()* function with a data.frame. The following code shows the step using the example input file "chr1Ped.csv".

```
> dName = system.file("extdata/example_ped.csv", package = "strum")
> dF = read.csv(dName, header=T)[,1:18]
> names(dF) = c("family","id", "father","mother",names(dF)[5:18])
> myAssoData = createStrumData(dF, "Pedigree")

 Creating strumData ............................. Done

> myAssoData
```

```
Data type: Pedigree
Data size: 477 entries, 18 variables

First 5 rows of data values:
  family id father mother sex disease proband         P1         P2         P3
1      1  1      0      0   0       0       0  0.4093955 0.44450079 -0.3867515
2      1  2      0      0   1       0       0 -1.5037814 1.52582608  0.8832360
3      1  3      1      2   0       0       0  1.5850090 0.08833692  0.9322619
4      1  4      1      2   1       0       0  1.6246356 0.60065352  1.0895325
5      1  5      1      2   1       0       0 -0.4111477 0.08588345 -0.6477336
    SBP     DBP     A1     A2      S1      S2 aSNP rs6040343
1  3.39  4.1800  1.300  1.630  1.9000 -0.0613    1         1
2 -3.49 -2.7200 -0.784 -3.550 -2.8900 -2.1300    0         0
3 -3.40  0.0815 -1.820 -4.390 -1.6700 -3.0900    1         0
4 -7.04 -3.6500 -0.183 -4.740 -2.9800 -2.3500    0         0
5  4.60  4.9900  2.440 -0.117 -0.0408 -0.4350    1         1

phi object contains  75  matrices:
First matrix:
$`1`
    1   2   3   4   5   6   7
1 1.0 0.0 0.5 0.5 0.5 0.5 0.5
2 0.0 1.0 0.5 0.5 0.5 0.5 0.5
3 0.5 0.5 1.0 0.5 0.5 0.5 0.5
4 0.5 0.5 0.5 1.0 0.5 0.5 0.5
5 0.5 0.5 0.5 0.5 1.0 0.5 0.5
6 0.5 0.5 0.5 0.5 0.5 1.0 0.5
7 0.5 0.5 0.5 0.5 0.5 0.5 1.0

Empty IBD object.
```

1.3 Run analysis

Now, run the association analysis by the function call *strum()* with two previously constructed objects as the arguments.

```
> myAssoResult = strum(myAssoModel, myAssoData)

 Start STRUM analysis ...
   Fitting model step 1 ......................... Done
   Fitting model step 2 ......................... Done
   Testing model fit ............................ Done

Analysis completed!
```

1.4 Result

The result object contains the model description and two result tables. The first table contains the fitted parameter values with standard errors, confidence intervals, and p-values. The second table contains the information on the model fit from four different measures. For association analysis, you would test H_0: $\gamma = 0$ versus H_1: $\gamma \neq 0$. In this model, γ is the parameter `L1 ~ aSNP`, which equals to 0.9445929 with the pvalue = 1.591018e-21.

```
> myAssoResult

=========
  Model
=========

Basic properties of the model:
         Model Class ............. strumFittedModel
         Ascertainment ..................... FALSE

List of all variables:
       Obs Covariate InEita   InY Exogen.
L1   FALSE     FALSE   TRUE FALSE   FALSE
aSNP  TRUE      TRUE  FALSE FALSE      NA
P1    TRUE     FALSE  FALSE  TRUE      NA
P2    TRUE     FALSE  FALSE  TRUE      NA
P3    TRUE     FALSE  FALSE  TRUE      NA

Model formulas:
  L1 =~ P1 + P2 + P3 + <e>
  L1 ~ aSNP + <p,e>


==========
  Result
==========

Parameter estimates:
                estimate   stdError     lowerCI   upperCI       pValue
L1=~P2         0.9885029 0.05314867  0.88433341 1.0926724 1.642115e-77
L1=~P3         1.0105280 0.05822325  0.89641252 1.1246435 8.869941e-68
L1~aSNP        0.9445929 0.09913024  0.75030117 1.1388846 7.955090e-22
P1~[intercept] 0.2880181 0.13404076  0.02530298 0.5507331 1.582771e-02
P2~[intercept] 0.1829933 0.13133455 -0.07441771 0.4404043 8.175896e-02
P3~[intercept] 0.3505190 0.12747443  0.10067375 0.6003643 2.982307e-03
P1~~P1<e>      1.1318519 0.18199793  0.77514251 1.4885613 2.501075e-10
P2~~P2<e>      1.2400615 0.14775629  0.95046454 1.5296585 2.377245e-17
P3~~P3<e>      0.6908993 0.19387808  0.31090526 1.0708934 1.829182e-04
```

```
L1~~L1<p>      0.9445110 0.26947683  0.41634613 1.4726759 2.283205e-04
L1~~L1<e>      1.1478948 0.20752417  0.74115493 1.5546347 1.588615e-08

Chi-square statistics of fit:
                            kappa   chiStat df     pValue
Un-adjusted             1.0000000  2.755859  7 0.99357480
Mean adjusted           0.2057025 13.397307  7 0.06299978
Mean-Variance adjusted  0.1599908 17.225108  9 0.04530531
Theoretically corrected 1.0000000 11.687927  7 0.11130000
```

2 Genetic linkage analysis

In this section, we show an example of a typical genetic linkage analysis model with a latent trait using IBD information. Suppose again that there are three measurements as above (P1, P2 and p3) and a single latent trait (L1) underlying the three measurements. The latent variable L1 is influenced by a set of genetic and random variance components. Each trait is also influenced by its own random environmental factor. The model diagram looks like following.

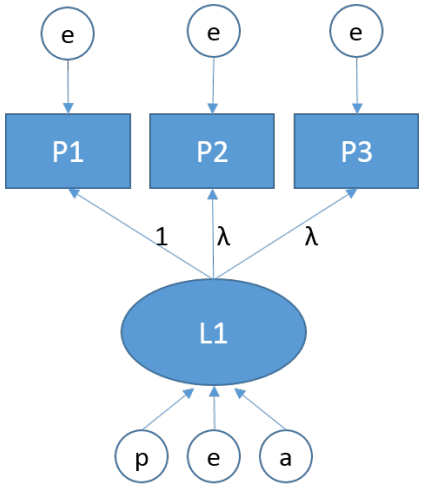

Figure 2: Genetic linkage analysis model

2.1 Construct model

The above linkage model can be constrcuted as a **strumModel** object using *createStrumModel()* function.

```
> linkForm1 =
+   'L1 =~ P1 + P2 + P3 + <e>
+    L1 ~ <a,p,e>
+   '
> myLinkModel = createStrumModel(formulas = linkForm1)

 Creating strumModel ............................. Done

> myLinkModel

Basic properties of the model:
         Model Class ................... strumModel
```

```
         Ascertainment ..................... FALSE

List of all variables:
     Obs Covariate InEita   InY Exogen.
L1 FALSE     FALSE   TRUE FALSE   FALSE
P1  TRUE     FALSE  FALSE  TRUE      NA
P2  TRUE     FALSE  FALSE  TRUE      NA
P3  TRUE     FALSE  FALSE  TRUE      NA

Model formulas:
  L1 =~ P1 + P2 + P3 + <e>
  L1 ~ <a,p,e>
```

2.2 Prepare data

From the above linkage analysis model, $\boldsymbol{a}$ represents the major gene variance components, which requires the ibd information to be imported. The ibd information for the family data can be imported by specifying the name of ibd file into *ibdFileName* argument for *createStrumData()*. The use of the example ibd file "GENIBD.chr1Ped.ibd", which contains the ibd information of family data in "chr1Ped.csv", is shown in the following code. We use the data.frame, dF, created for the previous association analysis model.

```
> iName = system.file("extdata/GENIBD.chr1Ped.ibd", package = "strum")
> myLinkData = createStrumData(dF, "Pedigree", ibdFileName=iName)

 Importing S.A.G.E. IBD file ..................... Done
 Creating strumData .............................. Done
```

2.3 Run analysis

Now, run the linkage analysis by the function call *strum()*. If you want to perform the linkage analysis on all markers exist in the IBD file, you don't need to specify the marker name as an argument for *strum()* function. In this case, each marker will be analysed one by one, and the result object will contain a list of the linkage analysis results for all markers.

```
> myLinkResultAll = strum(myLinkModel, myLinkData)
```

To analyze a subset of IBD markers, then you can specify the names of them as follows;

```
> mNames = c("chr1marker1", "chr1marker2")
> myLinkResult = strum(myLinkModel, myLinkData, ibdMarkers=mNames)

 Start STRUM analysis ...
```

```
  chr1marker1:
   Fitting model step 1 ......................... Done
   Fitting model step 2 ......................... Done
   Testing model fit ............................ Done

  chr1marker2:
   Fitting model step 1 ......................... Done
   Fitting model step 2 ......................... Done
   Testing model fit ............................ Done

Analysis completed!
```

2.4 Result

The result object again contains the model description and result tables. The first table contains the fitted parameter values with standard errors, confidence intervals, and p-values. The second table contains the information on the model fit from four different measures. For linkage analysis, you would test H_0: $\alpha = 0$ versus H_1: $\alpha \neq 0$. In this model, α is the parameter `L1` $\sim\sim$ `L1<a>`, which equals to 0.2787365 with the pvalue = 2.594076e-01.

```
> myLinkResult[[1]]

=========
  Model
=========

Basic properties of the model:
         Model Class ............. strumFittedModel
         Ascertainment ..................... FALSE

List of all variables:
     Obs Covariate InEita   InY Exogen.
L1 FALSE     FALSE   TRUE FALSE   FALSE
P1  TRUE     FALSE  FALSE  TRUE      NA
P2  TRUE     FALSE  FALSE  TRUE      NA
P3  TRUE     FALSE  FALSE  TRUE      NA

Model formulas:
  L1 =~ P1 + P2 + P3 + <e>
  L1 ~ <a,p,e>


==========
  Result
==========
```

```
Parameter estimates:
                 estimate   stdError    lowerCI  upperCI       pValue
L1=~P2         0.8678695 0.07590839  0.7190918 1.016647 1.428314e-30
L1=~P3         0.8910605 0.09321847  0.7083556 1.073765 5.954188e-22
P1~[intercept] 1.1238196 0.11825192  0.8920501 1.355589 1.013733e-21
P2~[intercept] 1.0432875 0.11808091  0.8118532 1.274722 4.988756e-19
P3~[intercept] 1.1673092 0.12331581  0.9256146 1.409004 1.453634e-21
P1~~P1<e>      0.8799191 0.30659124  0.2790113 1.480827 2.052312e-03
P2~~P2<e>      1.3934769 0.19780518  1.0057859 1.781168 9.293497e-13
P3~~P3<e>      0.6745702 0.21172640  0.2595941 1.089546 7.211563e-04
L1~~L1<p>      1.3114935 0.52174178  0.2888984 2.334089 5.973887e-03
L1~~L1<e>      1.4101136 0.35762894  0.7091738 2.111053 4.024244e-05
L1~~L1<a>      0.2787365 0.43203390 -0.5680344 1.125507 2.594076e-01

Chi-square statistics of fit:
                            kappa  chiStat df    pValue
Un-adjusted             1.0000000 3.295630 10 0.9862138
Mean adjusted           0.4177845 7.888349 10 0.6397420
Mean-Variance adjusted  0.3481538 9.466019 12 0.6626947
Theoretically corrected 1.0000000 9.054915 10 0.5269000
```

3 Structural Equation Model

This is an example of a SEM model with latent variables and polygeneic effect. Suppose that there are six measurements and three underline latent variables. anger is a latent variable which underlies the two measurements (A1, A2), bp is a latent variable which underlies the two measurements (SBP, DBP) and stress is a latent variable which underlies the two measurements (S1, S2). bp is caused by anger and stress, and stress is caused by anger and a SNP (rs6040343). All traits and latent variables are also influenced by their own polygenic and random variance components except stress, which the variance is fixed at 0.1 for both polygenic and random componants. The model diagram looks like following.

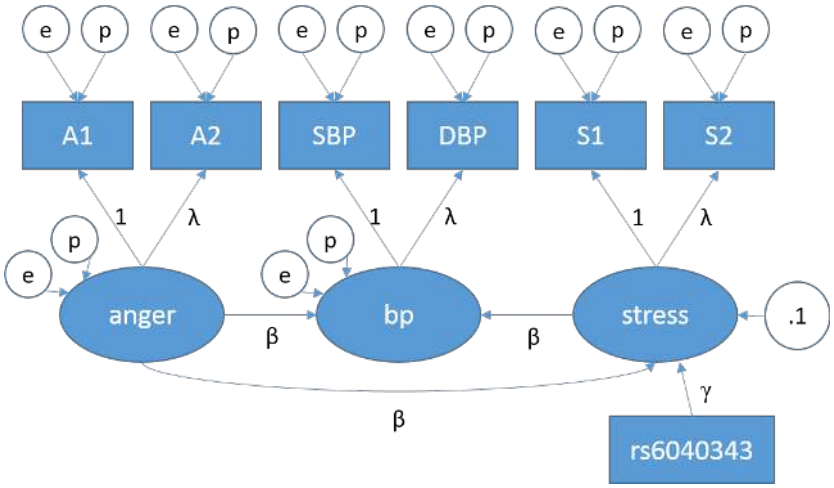

Figure 3: Structural equation model

3.1 Construct model

The above SEM model can be constrcuted as a **strumModel** object using *createStrumModel()* function.

```
> semForm1 =
+   'bp =~ SBP + DBP
+    anger =~ A1 + A2
+    stress =~ S1 + S2
+    bp ~ anger + stress
+    stress ~ anger + rs6040343
+    var(stress) = .1
+   '
> mySemModel = createStrumModel(formulas = semForm1)
```

```
 Creating strumModel ............................ Done
```

```
> mySemModel
```

```
Basic properties of the model:
         Model Class ................... strumModel
         Ascertainment ..................... FALSE

List of all variables:
            Obs Covariate InEita   InY Exogen.
bp        FALSE     FALSE   TRUE FALSE   FALSE
anger     FALSE     FALSE   TRUE FALSE    TRUE
stress    FALSE     FALSE   TRUE FALSE   FALSE
rs6040343  TRUE      TRUE  FALSE FALSE      NA
SBP        TRUE     FALSE  FALSE  TRUE      NA
DBP        TRUE     FALSE  FALSE  TRUE      NA
A1         TRUE     FALSE  FALSE  TRUE      NA
A2         TRUE     FALSE  FALSE  TRUE      NA
S1         TRUE     FALSE  FALSE  TRUE      NA
S2         TRUE     FALSE  FALSE  TRUE      NA

Model formulas:
  bp =~ SBP + DBP
  anger =~ A1 + A2
  stress =~ S1 + S2
  bp ~ anger + stress
  stress ~ anger + rs6040343
  var(stress) = .1
```

3.2 Prepare data

The next step is to prepare data. Note again that the data must be a data.frame with 4 required fields - family, id, father, mother, since the model includes the polygenic variance component (p) by default. A **strumData** object is created by *createStrumData()* function with a data.frame. Again, we use the data.frame, dF, created above using the example input file "chr1Ped.csv".

```
> mySemData = createStrumData(dF, "Pedigree")
```

```
 Creating strumData ............................ Done
```

```
> mySemData
```

```
Data type: Pedigree
Data size: 477 entries, 18 variables

First 5 rows of data values:
```

```
  family id father mother sex disease proband         P1         P2         P3
1      1  1      0      0   0       0       0  0.4093955 0.44450079 -0.3867515
2      1  2      0      0   1       0       0 -1.5037814 1.52582608  0.8832360
3      1  3      1      2   0       0       0  1.5850090 0.08833692  0.9322619
4      1  4      1      2   1       0       0  1.6246356 0.60065352  1.0895325
5      1  5      1      2   1       0       0 -0.4111477 0.08588345 -0.6477336
    SBP     DBP     A1     A2      S1      S2 aSNP rs6040343
1  3.39  4.1800  1.300  1.630  1.9000 -0.0613    1         1
2 -3.49 -2.7200 -0.784 -3.550 -2.8900 -2.1300    0         0
3 -3.40  0.0815 -1.820 -4.390 -1.6700 -3.0900    1         0
4 -7.04 -3.6500 -0.183 -4.740 -2.9800 -2.3500    0         0
5  4.60  4.9900  2.440 -0.117 -0.0408 -0.4350    1         1

phi object contains  75  matrices:
First matrix:
$`1`
    1   2   3   4   5   6   7
1 1.0 0.0 0.5 0.5 0.5 0.5 0.5
2 0.0 1.0 0.5 0.5 0.5 0.5 0.5
3 0.5 0.5 1.0 0.5 0.5 0.5 0.5
4 0.5 0.5 0.5 1.0 0.5 0.5 0.5
5 0.5 0.5 0.5 0.5 1.0 0.5 0.5
6 0.5 0.5 0.5 0.5 0.5 1.0 0.5
7 0.5 0.5 0.5 0.5 0.5 0.5 1.0

Empty IBD object.
```

3.3 Run analysis

Now, run the analysis by the function call *strum()* with two previously constructed objects as the arguments.

```
> mySemResult = strum(mySemModel, mySemData)

 Start STRUM analysis ...
   Fitting model step 1 ......................... Done
   Fitting model step 2 ......................... Done
   Testing model fit ............................ Done

Analysis completed!
```

3.4 Result

The result object again contains the model description and result tables. To test the SNP effect to stress, you would test H_0: $\gamma = 0$ versus H_1: $\gamma \neq 0$. In this model, γ is the parameter `stress` $\sim$ `rs6040343`, which equals to 1.013427436 with the pvalue = 2.000891e-12.

```
> mySemResult

=========
  Model
=========

Basic properties of the model:
         Model Class ............. strumFittedModel
         Ascertainment ..................... FALSE

List of all variables:
            Obs Covariate InEita   InY Exogen.
bp        FALSE     FALSE   TRUE FALSE   FALSE
anger     FALSE     FALSE   TRUE FALSE    TRUE
stress    FALSE     FALSE   TRUE FALSE   FALSE
rs6040343  TRUE      TRUE  FALSE FALSE      NA
SBP        TRUE     FALSE  FALSE  TRUE      NA
DBP        TRUE     FALSE  FALSE  TRUE      NA
A1         TRUE     FALSE  FALSE  TRUE      NA
A2         TRUE     FALSE  FALSE  TRUE      NA
S1         TRUE     FALSE  FALSE  TRUE      NA
S2         TRUE     FALSE  FALSE  TRUE      NA

Model formulas:
  bp =~ SBP + DBP
  anger =~ A1 + A2
  stress =~ S1 + S2
  bp ~ anger + stress
  stress ~ anger + rs6040343
  var(stress) = .1


==========
  Result
==========

Parameter estimates:
                     estimate   stdError     lowerCI   upperCI        pValue
bp=~DBP           1.035032179 0.04257460  0.95158749 1.1184769 7.494253e-131
anger=~A2         1.003172954 0.08028815  0.84581107 1.1605348  3.991982e-36
stress=~S2        1.055164012 0.08278765  0.89290320 1.2174248  1.652860e-37
bp~anger          0.823477033 0.19646223  0.43841813 1.2085359  1.385407e-05
stress~anger      0.942564975 0.07702239  0.79160386 1.0935261  9.793373e-35
bp~stress         1.052862533 0.16355422  0.73230215 1.3734229  6.077212e-11
stress~rs6040343  1.013427439 0.14608766  0.72710088 1.2997540  2.000891e-12
SBP~[intercept]  -0.117910321 0.30223817 -0.71028625 0.4744656  3.482225e-01
```

```
DBP~[intercept]  -0.302734409 0.30931966 -0.90898981 0.3035210  1.638615e-01
A1~[intercept]    0.018375753 0.22433007 -0.42130310 0.4580546  4.673576e-01
A2~[intercept]   -0.030596744 0.21819352 -0.45824819 0.3970547  4.442401e-01
S1~[intercept]    0.118914923 0.21176180 -0.29613058 0.5339604  2.872112e-01
S2~[intercept]    0.009989651 0.19519661 -0.37258867 0.3925680  4.795921e-01
SBP~~SBP<p>       0.477083699 0.51395234 -0.53024437 1.4844118  1.766352e-01
DBP~~DBP<p>       1.345743306 0.60224112  0.16537239 2.5261142  1.272316e-02
A1~~A1<p>         1.133010959 0.32774658  0.49063946 1.7753825  2.731402e-04
A2~~A2<p>         0.807655095 0.38678524  0.04956996 1.5657402  1.839338e-02
S1~~S1<p>         1.097210967 0.39553172  0.32198304 1.8724389  2.768455e-03
S2~~S2<p>         0.680742254 0.35435561 -0.01378198 1.3752665  2.736139e-02
SBP~~SBP<e>       1.259787416 0.30649356  0.65907107 1.8605038  1.975534e-05
DBP~~DBP<e>       0.624278085 0.36314414 -0.08747134 1.3360275  4.279883e-02
A1~~A1<e>         0.702376222 0.20543107  0.29973873 1.1050137  3.142170e-04
A2~~A2<e>         1.225357638 0.27516889  0.68603652 1.7646788  4.231747e-06
S1~~S1<e>         1.273773005 0.25233960  0.77919648 1.7683495  2.234023e-07
S2~~S2<e>         1.234330770 0.25197404  0.74047073 1.7281908  4.825049e-07
bp~~bp<p>         0.586876883 0.60011805 -0.58933288 1.7630866  1.640531e-01
anger~~anger<p>   1.154779475 0.25292433  0.65905691 1.6505020  2.489016e-06
bp~~bp<e>         1.078347720 0.40995946  0.27484194 1.8818535  4.264518e-03
anger~~anger<e>   0.886146282 0.19375800  0.50638758 1.2659050  2.398569e-06

Chi-square statistics of fit:
                            kappa   chiStat df    pValue
Un-adjusted             1.0000000  7.407714 25 0.9999831
Mean adjusted           0.5440739 13.615273 25 0.9680314
Mean-Variance adjusted  0.4857802 15.249105 28 0.9756850
Theoretically corrected 1.0000000 18.067778 25 0.8395000
```

4 SessionInfo

```
> sessionInfo();

R version 3.1.2 (2014-10-31)
Platform: x86_64-w64-mingw32/x64 (64-bit)

locale:
[1] LC_COLLATE=English_United States.1252
[2] LC_CTYPE=English_United States.1252
[3] LC_MONETARY=English_United States.1252
[4] LC_NUMERIC=C
[5] LC_TIME=English_United States.1252

attached base packages:
[1] grid      stats     graphics  grDevices utils     datasets  methods
[8] base

other attached packages:
[1] strum_0.4        Rgraphviz_2.10.0 graph_1.44.1     pedigree_1.4
[5] reshape_0.8.5    HaploSim_1.8.4   Matrix_1.1-4

loaded via a namespace (and not attached):
[1] BiocGenerics_0.12.1 lattice_0.20-29     MASS_7.3-35
[4] parallel_3.1.2      plyr_1.8.1          Rcpp_0.11.3
[7] stats4_3.1.2        tools_3.1.2
```

References

Morris, N.J., Elston, R.C., & Stein, C.M. (2010). A framework for structural equation models in general pedigrees. *Human heredity*, 70, 278–286.