

Reference Manual for Set-Valued System Identification (SVSI) Analysis

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1 Overview

Set-Valued System Identification analysis attempts to test genetic associations with complex phenotypes such as ordered categorical phenotype [1] or binary phenotype [2] based on set-valued model and using a novel Set-Valued System Identification algorithm. Basically, the set-valued model models the classification/dichotomization process of a continuous complicated unobserved or unobservable phenotype and models the relationship between categorical outcome and genetic variants. Set-Valued System Identification (SVSI) algorithm is a new algorithm based on expectation-maximization (EM) which has been proposed and appears in a wide range of applications such as sensor networks and telecommunications.

In this document, we describe how to perform SVSI analysis for ordered categorical phenotype and binary phenotype using example data sets provided with the package.

2 Installation

The latest version of SVSI package can be download from

<http://www.stjudereresearch.org/site/depts/biostats/software>.

```
> # Install packages
> # Load the package
> library(SVSI)
```

3 Testing associations between SNPs and an ordered categorical phenotype

3.1 Example dataset

SVSI package provides an example dataset (`data_cate_geno`) which has a genotype matrix of 697 individuals and 20 SNPs among which the last 10 SNPs are generated from the alternative hypothesis, two binary and one continuous covariates (`data_cate_cova`).

```
> # Install packages
> # Load the package
> library(SVSI)
> # Load the example data set
> data(data_cate_geno) #ordered categorical outcome data and genotype data
> data(data_cate_cova) #covariate data for categorical outcome data
> names(data_cate_geno)#colnames of data_cate_geno
```

```

[1] "FID"      "IID"      "PAT"      "MAT"      "SEX"      "status"   "SNP1"     "SNP2"
[9] "SNP3"     "SNP4"     "SNP5"     "SNP6"     "SNP7"     "SNP8"     "SNP9"     "SNP10"
[17] "SNP11"    "SNP12"    "SNP13"    "SNP14"    "SNP15"    "SNP16"    "SNP17"    "SNP18"
[25] "SNP19"    "SNP20"

```

```
> names(data_cate_cova)#colnames of data_cate_cova
```

```
[1] "FID"      "IID"      "SEX"      "AGE"      "SMOKE"
```

```
> summary(data_cate_genotype)#summary of data_cate_genotype
```

| FID | IID | PAT | MAT | SEX |
|------------------|------------------|------------------|------------------|---------------|
| Length:697 | Min. :1 | Min. :0 | Min. :0 | Min. :1.000 |
| Class :character | 1st Qu.:1 | 1st Qu.:0 | 1st Qu.:0 | 1st Qu.:1.000 |
| Mode :character | Median :1 | Median :0 | Median :0 | Median :2.000 |
| | Mean :1 | Mean :0 | Mean :0 | Mean :1.531 |
| | 3rd Qu.:1 | 3rd Qu.:0 | 3rd Qu.:0 | 3rd Qu.:2.000 |
| | Max. :1 | Max. :0 | Max. :0 | Max. :2.000 |
| status | SNP1 | SNP2 | SNP3 | |
| Min. :0.0000 | Min. :0.000000 | Min. :0.000000 | Min. :0.000000 | |
| 1st Qu.:0.0000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | |
| Median :0.0000 | Median :0.000000 | Median :0.000000 | Median :0.000000 | |
| Mean :0.4878 | Mean :0.007174 | Mean :0.02869 | Mean :0.01004 | |
| 3rd Qu.:1.0000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | |
| Max. :2.0000 | Max. :1.000000 | Max. :2.000000 | Max. :1.000000 | |
| SNP4 | SNP5 | SNP6 | SNP7 | |
| Min. :0.000000 | Min. :0.000000 | Min. :0.000000 | Min. :0.000000 | |
| 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | |
| Median :0.000000 | Median :0.000000 | Median :0.000000 | Median :0.000000 | |
| Mean :0.002869 | Mean :0.004304 | Mean :0.01435 | Mean :0.008608 | |
| 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | |
| Max. :1.000000 | Max. :1.000000 | Max. :2.000000 | Max. :2.000000 | |
| SNP8 | SNP9 | SNP10 | SNP11 | |
| Min. :0.000000 | Min. :0.000000 | Min. :0.000000 | Min. :0.000000 | |
| 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | |
| Median :0.000000 | Median :0.000000 | Median :0.000000 | Median :0.000000 | |
| Mean :0.002869 | Mean :0.007174 | Mean :0.007174 | Mean :0.01291 | |
| 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | |
| Max. :1.000000 | Max. :2.000000 | Max. :1.000000 | Max. :1.000000 | |
| SNP12 | SNP13 | SNP14 | SNP15 | |
| Min. :0.0000 | Min. :0.000000 | Min. :0.000000 | Min. :0.000000 | |
| 1st Qu.:0.0000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | |
| Median :0.0000 | Median :0.000000 | Median :0.000000 | Median :0.000000 | |
| Mean :0.2912 | Mean :0.002869 | Mean :0.03443 | Mean :0.01004 | |
| 3rd Qu.:1.0000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | |
| Max. :2.0000 | Max. :1.000000 | Max. :2.000000 | Max. :2.000000 | |
| SNP16 | SNP17 | SNP18 | SNP19 | |
| Min. :0.000000 | Min. :0.000 | Min. :0.000000 | Min. :0.000000 | |
| 1st Qu.:0.000000 | 1st Qu.:0.000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | |
| Median :0.000000 | Median :0.000 | Median :0.000000 | Median :0.000000 | |
| Mean :0.002869 | Mean :0.066 | Mean :0.01722 | Mean :0.005739 | |
| 3rd Qu.:0.000000 | 3rd Qu.:0.000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | |

```

Max. :1.000000 Max. :2.000 Max. :1.00000 Max. :1.000000
SNP20
Min. :0.000000
1st Qu.:0.000000
Median :0.000000
Mean :0.002869
3rd Qu.:0.000000
Max. :1.000000

```

```
> summary(data_cate_cova)#summary of data_cate_cova
```

```

      FID          IID          SEX          AGE
Length:697      Min.   :1      Min.   :1.000      Min.   :16.00
Class :character 1st Qu.:1      1st Qu.:1.000      1st Qu.:25.00
Mode  :character Median :1      Median :2.000      Median :40.00
      Mean   :1      Mean   :1.531      Mean   :41.79
      3rd Qu.:1      3rd Qu.:2.000      3rd Qu.:52.00
      Max.   :1      Max.   :2.000      Max.   :91.00

```

```
SMOKE
```

```

Min. :0.0000
1st Qu.:0.0000
Median :0.0000
Mean :0.2597
3rd Qu.:1.0000
Max. :1.0000

```

```
> print(data_cate_gen0[1:3,]) #display the first three rows of data_cate_gen0
```

```

      FID IID PAT MAT SEX status SNP1 SNP2 SNP3 SNP4 SNP5 SNP6 SNP7 SNP8 SNP9 SNP10
1 ID1  1  0  0  1    0    0  1  0  0  0  0  0  0  0  1  0
2 ID2  1  0  0  2    2    0  0  0  0  0  0  0  0  0  0  0
3 ID3  1  0  0  2    0    0  0  0  0  0  0  0  0  0  0  0
      SNP11 SNP12 SNP13 SNP14 SNP15 SNP16 SNP17 SNP18 SNP19 SNP20
1    0    0    0    0    0    0    0    0    0    0
2    0    0    0    0    0    0    0    0    0    0
3    0    1    0    0    0    0    0    0    0    0

```

```
> print(data_cate_cova[1:3,]) #display the first three rows of data_cate_cova
```

```

      FID IID SEX AGE SMOKE
1 ID1  1  1  82    0
2 ID2  1  2  86    0
3 ID3  1  2  84    1

```

3.2 Genetic association test with adjusting for covariates using SVSI

Conduct genetic association testing on the input data (data_cate_gen0) with adjusting for covariate (data_cate_cova):

```

> out=SVSI_OrderCate_Whole(data_cate_gen0,data_cate_cova,prefix="",result.dir=NA)
> out[,1:6]

```

| | [,1] | [,2] | [,3] | [,4] | [,5] | [,6] |
|-------|---------|------------|-------------|------------|------------|------------|
| | " | "Variable" | "Estimate" | "SE" | "Stat" | "Pval" |
| SNP1 | "SNP1" | "geno" | " 0.735100" | "0.50340" | "2.133" | "0.1442" |
| SNP2 | "SNP2" | "geno" | "-0.765600" | "0.350800" | "4.7640" | "0.02907" |
| SNP3 | "SNP3" | "geno" | "-2.657000" | "3.179000" | "0.6984" | "0.4033" |
| SNP4 | "SNP4" | "geno" | "-2.641000" | "5.948000" | "0.1972" | "0.6570" |
| SNP5 | "SNP5" | "geno" | "-2.791000" | "4.814000" | "0.3360" | "0.5621" |
| SNP6 | "SNP6" | "geno" | " 0.378300" | "0.304000" | "1.549" | "0.2133" |
| SNP7 | "SNP7" | "geno" | "-0.242700" | "0.467000" | "0.2700" | "0.6033" |
| SNP8 | "SNP8" | "geno" | " 0.085240" | "0.841500" | "0.01026" | "0.9193" |
| SNP9 | "SNP9" | "geno" | "-1.846000" | "3.078000" | "0.3599" | "0.5486" |
| SNP10 | "SNP10" | "geno" | "-2.667000" | "3.75300" | "0.5050" | "0.4773" |
| SNP11 | "SNP11" | "geno" | " 0.971000" | "0.378000" | "6.5980" | "0.01021" |
| SNP12 | "SNP12" | "geno" | " 0.007681" | "0.090120" | "0.007265" | "0.9321" |
| SNP13 | "SNP13" | "geno" | "-2.658000" | "5.940000" | "0.2003" | "0.6545" |
| SNP14 | "SNP14" | "geno" | "-0.305000" | "0.260700" | "1.3690" | "0.2421" |
| SNP15 | "SNP15" | "geno" | " 0.307800" | "0.31300" | "0.9671" | "0.3254" |
| SNP16 | "SNP16" | "geno" | "-2.809000" | "5.919000" | "0.2252" | "0.6351" |
| SNP17 | "SNP17" | "geno" | "-0.110500" | "0.17620" | "0.3936" | "0.5304" |
| SNP18 | "SNP18" | "geno" | " 0.913900" | "0.328300" | "7.749" | "0.005373" |
| SNP19 | "SNP19" | "geno" | " 0.080910" | "0.596100" | "0.01842" | "0.8920" |
| SNP20 | "SNP20" | "geno" | " 0.860600" | "0.792800" | "1.1780" | "0.2777" |

3.3 Genetic association test without adjusting for covariates using SVSI

Conduct genetic association testing on the input data (`data_cate_gen`) without adjusting for any covariate:

```
> out=SVSI_OrderCate_Whole(data_cate_gen,data_cate_cova=NA)
> out
```

| | [,1] | [,2] | [,3] | [,4] | [,5] | [,6] |
|-------|---------|------------|------------|-----------|------------|------------|
| | " | "Variable" | "Estimate" | "SE" | "Stat" | "Pval" |
| SNP1 | "SNP1" | "geno" | "0.7858" | "0.5015" | "2.455" | "0.1172" |
| SNP2 | "SNP2" | "geno" | "-0.7582" | "0.3467" | "4.781" | "0.02877" |
| SNP3 | "SNP3" | "geno" | "-2.782" | "3.423" | "0.6606" | "0.4164" |
| SNP4 | "SNP4" | "geno" | "-2.775" | "6.404" | "0.1877" | "0.6648" |
| SNP5 | "SNP5" | "geno" | "-2.776" | "5.229" | "0.2818" | "0.5955" |
| SNP6 | "SNP6" | "geno" | "0.3518" | "0.3031" | "1.348" | "0.2457" |
| SNP7 | "SNP7" | "geno" | "-0.2108" | "0.458" | "0.2119" | "0.6453" |
| SNP8 | "SNP8" | "geno" | "0.06611" | "0.8391" | "0.006207" | "0.9372" |
| SNP9 | "SNP9" | "geno" | "-1.896" | "3.188" | "0.3535" | "0.5521" |
| SNP10 | "SNP10" | "geno" | "-2.779" | "4.05" | "0.4708" | "0.4926" |
| SNP11 | "SNP11" | "geno" | "0.9571" | "0.3761" | "6.476" | "0.01093" |
| SNP12 | "SNP12" | "geno" | "0.007383" | "0.08981" | "0.006758" | "0.9345" |
| SNP13 | "SNP13" | "geno" | "-2.775" | "6.404" | "0.1877" | "0.6648" |
| SNP14 | "SNP14" | "geno" | "-0.3143" | "0.2597" | "1.465" | "0.2261" |
| SNP15 | "SNP15" | "geno" | "0.3065" | "0.3123" | "0.9638" | "0.3262" |
| SNP16 | "SNP16" | "geno" | "-2.775" | "6.404" | "0.1877" | "0.6648" |
| SNP17 | "SNP17" | "geno" | "-0.1025" | "0.1754" | "0.3411" | "0.5592" |
| SNP18 | "SNP18" | "geno" | "0.9155" | "0.3261" | "7.884" | "0.004986" |

```
SNP19 "SNP19" "geno"      "0.06632" "0.5942" "0.01245" "0.9111"
SNP20 "SNP20" "geno"      "0.7809"  "0.791"  "0.9746"  "0.3235"
```

4 Testing associations between SNPs and a binary phenotype

4.1 Example dataset

SVSI package provides an example dataset (`data_bina_gen`) which has a genotype matrix of 697 individuals and 20 SNPs among which the last 2 SNPs are generated from the alternative hypothesis, two binary and one continuous covariates (`data_bina_cov`).

```
> # Install packages
> # Load the package
> library(SVSI)
> # Load the example data set
> data(data_bina_gen) #ordered binagorical outcome data and genotype data
> data(data_bina_cov) #covariate data for binagorical outcome data
> names(data_bina_gen)#colname of data_bina_gen

 [1] "FID"      "IID"      "PAT"      "MAT"      "SEX"      "status"   "SNP1"     "SNP2"
 [9] "SNP3"     "SNP4"     "SNP5"     "SNP6"     "SNP7"     "SNP8"     "SNP9"     "SNP10"
[17] "SNP11"    "SNP12"    "SNP13"    "SNP14"    "SNP15"    "SNP16"    "SNP17"    "SNP18"
[25] "SNP19"    "SNP20"
```

```
> names(data_bina_cov)#colname of data_bina_cov

[1] "FID"      "IID"      "SEX"      "AGE"      "SMOKE"
```

```
> summary(data_bina_gen)#summary of data_bina_gen
```

| FID | IID | PAT | MAT | SEX |
|------------------|-----------|-----------|-----------|---------------|
| Length:697 | Min. :1 | Min. :0 | Min. :0 | Min. :1.000 |
| Class :character | 1st Qu.:1 | 1st Qu.:0 | 1st Qu.:0 | 1st Qu.:1.000 |
| Mode :character | Median :1 | Median :0 | Median :0 | Median :2.000 |
| | Mean :1 | Mean :0 | Mean :0 | Mean :1.531 |
| | 3rd Qu.:1 | 3rd Qu.:0 | 3rd Qu.:0 | 3rd Qu.:2.000 |
| | Max. :1 | Max. :0 | Max. :0 | Max. :2.000 |

| status | SNP1 | SNP2 | SNP3 |
|----------------|------------------|------------------|------------------|
| Min. :0.0000 | Min. :0.000000 | Min. :0.000000 | Min. :0.000000 |
| 1st Qu.:0.0000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 |
| Median :0.0000 | Median :0.000000 | Median :0.000000 | Median :0.000000 |
| Mean :0.2999 | Mean :0.007174 | Mean :0.02869 | Mean :0.01004 |
| 3rd Qu.:1.0000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 |
| Max. :1.0000 | Max. :1.000000 | Max. :2.000000 | Max. :1.000000 |

| SNP4 | SNP5 | SNP6 | SNP7 |
|------------------|------------------|------------------|------------------|
| Min. :0.000000 | Min. :0.000000 | Min. :0.000000 | Min. :0.000000 |
| 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 | 1st Qu.:0.000000 |
| Median :0.000000 | Median :0.000000 | Median :0.000000 | Median :0.000000 |
| Mean :0.002869 | Mean :0.004304 | Mean :0.01435 | Mean :0.008608 |
| 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 | 3rd Qu.:0.000000 |
| Max. :1.000000 | Max. :1.000000 | Max. :2.000000 | Max. :2.000000 |

| SNP8 | | SNP9 | | SNP10 | | SNP11 | |
|---------|-----------|---------|-----------|---------|-----------|---------|-----------|
| Min. | :0.000000 | Min. | :0.000000 | Min. | :0.000000 | Min. | :0.000000 |
| 1st Qu. | :0.000000 | 1st Qu. | :0.000000 | 1st Qu. | :0.000000 | 1st Qu. | :0.000000 |
| Median | :0.000000 | Median | :0.000000 | Median | :0.000000 | Median | :0.000000 |
| Mean | :0.002869 | Mean | :0.04304 | Mean | :0.002869 | Mean | :0.002869 |
| 3rd Qu. | :0.000000 | 3rd Qu. | :0.000000 | 3rd Qu. | :0.000000 | 3rd Qu. | :0.000000 |
| Max. | :1.000000 | Max. | :2.00000 | Max. | :1.000000 | Max. | :1.000000 |
| SNP12 | | SNP13 | | SNP14 | | SNP15 | |
| Min. | :0.000000 | Min. | :0.000000 | Min. | :0.000000 | Min. | :0.000000 |
| 1st Qu. | :0.000000 | 1st Qu. | :0.000000 | 1st Qu. | :0.000000 | 1st Qu. | :0.000000 |
| Median | :0.000000 | Median | :0.000000 | Median | :0.000000 | Median | :0.000000 |
| Mean | :0.01578 | Mean | :0.004304 | Mean | :0.05882 | Mean | :0.002869 |
| 3rd Qu. | :0.000000 | 3rd Qu. | :0.000000 | 3rd Qu. | :0.000000 | 3rd Qu. | :0.000000 |
| Max. | :1.00000 | Max. | :1.000000 | Max. | :2.00000 | Max. | :1.000000 |
| SNP16 | | SNP17 | | SNP18 | | SNP19 | |
| Min. | :0.0000 | Min. | :0.000000 | Min. | :0.000000 | Min. | :0.0000 |
| 1st Qu. | :0.0000 | 1st Qu. | :0.000000 | 1st Qu. | :0.000000 | 1st Qu. | :0.0000 |
| Median | :0.0000 | Median | :0.000000 | Median | :0.000000 | Median | :0.0000 |
| Mean | :0.3831 | Mean | :0.02152 | Mean | :0.005739 | Mean | :0.1334 |
| 3rd Qu. | :1.0000 | 3rd Qu. | :0.000000 | 3rd Qu. | :0.000000 | 3rd Qu. | :0.0000 |
| Max. | :2.0000 | Max. | :1.00000 | Max. | :1.000000 | Max. | :1.0000 |
| SNP20 | | | | | | | |
| Min. | :0.000000 | | | | | | |
| 1st Qu. | :0.000000 | | | | | | |
| Median | :0.000000 | | | | | | |
| Mean | :0.05595 | | | | | | |
| 3rd Qu. | :0.000000 | | | | | | |
| Max. | :1.000000 | | | | | | |

```
> summary(data_bina_cova)#summary of data_bina_cova
```

| FID | IID | SEX | AGE |
|------------------|-----------|----------------|---------------|
| Length:697 | Min. :1 | Min. :0.0000 | Min. :16.00 |
| Class :character | 1st Qu.:1 | 1st Qu.:0.0000 | 1st Qu.:25.00 |
| Mode :character | Median :1 | Median :1.0000 | Median :40.00 |
| | Mean :1 | Mean :0.5308 | Mean :41.79 |
| | 3rd Qu.:1 | 3rd Qu.:1.0000 | 3rd Qu.:52.00 |
| | Max. :1 | Max. :1.0000 | Max. :91.00 |

```
SMOKE
Min. :0.0000
1st Qu.:0.0000
Median :0.0000
Mean :0.2425
3rd Qu.:0.0000
Max. :1.0000
```

```
> print(data_bina_gen0[1:3,]) #display the first three rows of data_bina_gen0
```

| | FID | IID | PAT | MAT | SEX | status | SNP1 | SNP2 | SNP3 | SNP4 | SNP5 | SNP6 | SNP7 | SNP8 | SNP9 | SNP10 |
|---|-----|-----|-----|-----|-----|--------|------|------|------|------|------|------|------|------|------|-------|
| 1 | ID1 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | ID2 | 1 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | ID3 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

```

  SNP11 SNP12 SNP13 SNP14 SNP15 SNP16 SNP17 SNP18 SNP19 SNP20
1      0      0      0      1      0      1      0      0      0      0
2      0      0      0      0      0      1      0      0      0      0
3      0      0      0      0      0      0      0      0      0      0

```

```
> print(data_bina_cova[1:3,]) #display the first three rows of data_bina_cova
```

```

  FID IID SEX AGE SMOKE
1 ID1  1  0 82   0
2 ID2  1  1 86   0
3 ID3  1  1 84   0

```

4.2 Genetic association test with adjusting for covariates using SVSI

Conduct genetic association testing on the input data (`data_bina_gen`) with adjusting for covariate (`data_bina_cova`):

```
> out=SVSI_Bina_Whole(data_bina_gen,data_bina_cova)
> out[,1:6]
```

| | [,1] | [,2] | [,3] | [,4] | [,5] | [,6] |
|-------|---------|------------|------------|-----------|-----------|-------------|
| | " | "Variable" | "Estimate" | "SE" | "Stat" | "Pval" |
| SNP1 | "SNP1" | "geno" | "-1.077" | "0.6357" | "2.87" | "0.09027" |
| SNP2 | "SNP2" | "geno" | "0.4505" | "0.3391" | "1.765" | "0.184" |
| SNP3 | "SNP3" | "geno" | "0.1673" | "0.5342" | "0.09815" | "0.7541" |
| SNP4 | "SNP4" | "geno" | "-0.187" | "0.9583" | "0.03809" | "0.8453" |
| SNP5 | "SNP5" | "geno" | "-0.2635" | "0.8461" | "0.097" | "0.7555" |
| SNP6 | "SNP6" | "geno" | "0.06807" | "0.3769" | "0.03262" | "0.8567" |
| SNP7 | "SNP7" | "geno" | "0.3829" | "0.5616" | "0.4648" | "0.4954" |
| SNP8 | "SNP8" | "geno" | "3.469" | "8.931" | "0.1509" | "0.6977" |
| SNP9 | "SNP9" | "geno" | "0.3005" | "0.2652" | "1.284" | "0.2571" |
| SNP10 | "SNP10" | "geno" | "2.812" | "9.129" | "0.09487" | "0.7581" |
| SNP11 | "SNP11" | "geno" | "2.998" | "9.002" | "0.1109" | "0.7391" |
| SNP12 | "SNP12" | "geno" | "0.2289" | "0.4629" | "0.2445" | "0.621" |
| SNP13 | "SNP13" | "geno" | "2.123" | "7.446" | "0.0813" | "0.7755" |
| SNP14 | "SNP14" | "geno" | "0.04715" | "0.2184" | "0.04662" | "0.8291" |
| SNP15 | "SNP15" | "geno" | "-0.5882" | "0.916" | "0.4124" | "0.5208" |
| SNP16 | "SNP16" | "geno" | "0.06238" | "0.09372" | "0.443" | "0.5057" |
| SNP17 | "SNP17" | "geno" | "0.3464" | "0.4094" | "0.7158" | "0.3975" |
| SNP18 | "SNP18" | "geno" | "-0.3562" | "0.6647" | "0.2872" | "0.592" |
| SNP19 | "SNP19" | "geno" | "-0.6177" | "0.1555" | "15.78" | "7.125e-05" |
| SNP20 | "SNP20" | "geno" | "-0.9028" | "0.2253" | "16.05" | "6.158e-05" |

4.3 Genetic association test without adjusting for covariates using SVSI

Conduct genetic association testing on the input data (`data_bina_gen`) without adjusting for covariate:

```
> out=SVSI_Bina_Whole(data_bina_gen,data_bina_cova=NA)
> out
```

| | [,1] | [,2] | [,3] | [,4] | [,5] | [,6] |
|--|------|------------|------------|------|--------|--------|
| | " | "Variable" | "Estimate" | "SE" | "Stat" | "Pval" |

| | | | | | | |
|-------|---------|--------|--------------|-----------|-------------|-------------|
| SNP1 | "SNP1" | "geno" | "-0.7844" | "0.5693" | "1.898" | "0.1682" |
| SNP2 | "SNP2" | "geno" | "0.1221" | "0.2719" | "0.2016" | "0.6534" |
| SNP3 | "SNP3" | "geno" | "-0.3486" | "0.4791" | "0.5292" | "0.4669" |
| SNP4 | "SNP4" | "geno" | "-0.5265" | "0.8876" | "0.3518" | "0.5531" |
| SNP5 | "SNP5" | "geno" | "-0.0945" | "0.7502" | "0.01587" | "0.8998" |
| SNP6 | "SNP6" | "geno" | "-0.0002912" | "0.3541" | "6.762e-07" | "0.9993" |
| SNP7 | "SNP7" | "geno" | "0.3542" | "0.5474" | "0.4186" | "0.5176" |
| SNP8 | "SNP8" | "geno" | "2.785" | "9.131" | "0.09305" | "0.7603" |
| SNP9 | "SNP9" | "geno" | "-0.0003642" | "0.2237" | "2.65e-06" | "0.9987" |
| SNP10 | "SNP10" | "geno" | "2.785" | "9.131" | "0.09305" | "0.7603" |
| SNP11 | "SNP11" | "geno" | "2.785" | "9.131" | "0.09305" | "0.7603" |
| SNP12 | "SNP12" | "geno" | "-0.179" | "0.3896" | "0.2111" | "0.6459" |
| SNP13 | "SNP13" | "geno" | "2.787" | "7.456" | "0.1397" | "0.7086" |
| SNP14 | "SNP14" | "geno" | "-0.04427" | "0.1956" | "0.05123" | "0.8209" |
| SNP15 | "SNP15" | "geno" | "-0.5265" | "0.8876" | "0.3518" | "0.5531" |
| SNP16 | "SNP16" | "geno" | "-0.02228" | "0.08365" | "0.07096" | "0.7899" |
| SNP17 | "SNP17" | "geno" | "0.1002" | "0.3511" | "0.08145" | "0.7753" |
| SNP18 | "SNP18" | "geno" | "-0.5281" | "0.6287" | "0.7058" | "0.4008" |
| SNP19 | "SNP19" | "geno" | "-0.4073" | "0.1415" | "8.284" | "0.003999" |
| SNP20 | "SNP20" | "geno" | "-0.7318" | "0.2082" | "12.35" | "0.0004401" |

5 Contact Information

If you have any technique questions about using the SVSI package, please email us at: guolian.kang@stjude.org or biwenjian@amss.ac.cn or zhifa.liu@stjude.org.

References

- [1] Wenjian Bi, Guolian Kang, Yanlong Zhao, Yuehua Cui, Song Yan, Yun Li, Cheng Cheng, Stanley B. Pounds, Michael J. Borowitz, Mary V. Relling, Jun J. Yang, Ching-Hon Pui, Stephen P. Hunger, Christine M Hartford, Wing Leung, Ji-Feng Zhang. (2014). SVSI: Fast and Powerful Set-Valued System Identification Approach to Identifying Rare Variants in Sequencing Studies for Ordered Categorical Traits. *Annals of Human Genetics* **Accepted with a major revision**.
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