

# An Introduction to *POST*

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## 1 Introduction

POST, Projection onto Orthogonal Space Test, is a general procedure to test a set of genomic features that exhibit association with an endpoint variable. For each gene-set, POST represents the gene profiles as a set of eigenvectors and then uses statistical modeling to compute a set of (adjusted) z-statistics that measure the association of each eigenvector with the phenotype. The overall gene-set statistic is the sum of squared z-statistics weighted by the corresponding eigenvector. Finally, bootstrapping is used to compute a *p*-value.

In this document, we describe how to perform POST procedure using hypothetical example data sets provided with the package.

## 2 Requirements

The POST package depends on *Biobase*, *GSEABase*, *CompQuadForm* and *Matrix*. The understanding of *ExpressionSet* and *GeneSetCollection* is a prerequisite to perform the POST procedure.

The detailed requirements are illustrated below.

Load the POST package and the example data sets: `sampExprSet` and `exmplGeneSet` into R.

```
> library(POST)
> data(sampExprSet)
> data(sampGeneSet)
```

The *ExpressionSet* should contain at least two components: *exprs* (array data) and *phenoData* (endpoint data). *exprs* is a data frame with column names representing the array identifiers (IDs) and row names representing the probe (genomic feature) IDs. *phenoData* is an *AnnotatedDataFrame* with column names representing the endpoint variables and row names representing array. The array IDs of *phenoData* and *exprs* should be matched.

*GeneSetCollection* contains gene set definition. This gene set collection can be from biological processes or ontologies. In this hypothetical example, we are interested in testing association of expression of 4 gene sets with a binary outcome and association of expression of gene sets with a time-to-event endpoint.

### 3 POST Analysis

As mentioned in section 2, the *ExpressionSet* and *GeneSetCollection* are required by POST procedure. The code below performs a POST analysis at gene set level to detect association of gene set with binary outcome in logistic regression framework.

```
> test<-POSTglm(exprSet=sampExprSet,
+               geneSet=sampGeneSet,
+               lamda=0.95,
+               seed=13,
+               nboots=100,
+               model='Group ~ ',
+               family=binomial(link = "logit"))
```

Gene set result:

```
> test

      GeneSet Nprobe Nproj Stat
[1,] "SetA"   "10"   "4"   "2.42341946595234"
[2,] "SetB"   "10"   "4"   "63.6341928599234"
[3,] "SetC"   "10"   "5"   "40.4788851952684"
[4,] "SetD"   "30"   "4"   "58.9759176199774"
      p.value
[1,] "0.738735024903039"
[2,] "0.00166225382835439"
[3,] "0.0195953770210455"
[4,] "0.142760313270624"
```

The code below performs POST analysis at gene set level to detect association of gene set with time to event endpoint in Cox proportional hazard model framework.

```
> test2<-POSTcoxph(exprSet=sampExprSet,
+                  geneSet=sampGeneSet,
+                  lamda=0.95,
+                  nboots=100,
+                  model="Surv(time, censor) ~ ",
+                  seed=13)
```

```
> test2

      GeneSet Nprobe Nproj Stat
[1,] "SetA"   "10"   "4"   "6.73347880247785"
[2,] "SetB"   "10"   "4"   "10.7974608126469"
[3,] "SetC"   "10"   "5"   "11.2005143113062"
[4,] "SetD"   "30"   "4"   "13.8964097387099"
```

```
      p.value  
[1,] "0.354932076148768"  
[2,] "0.248238953750029"  
[3,] "0.367212521285667"  
[4,] "0.57770769131475"
```