MantelCorr Package for Bioconductor

Brian Steinmeyer, MS, and William Shannon, PhD
Department of Internal Medicine
Division of General Medical Sciences
Washington University in St. Louis
School of Medicine
e-mail: steinmeb@ilya.wustl.edu, wshannon@wustl.edu
April 30, 2008

Contents

1 Description 1

2 Example R session with the Golub training data 2

3 Reminder 2

4 GetClusters() function 2

5 DistMatrices() function 2

6 MantelCorrs() function 3

7 PermutationTest() function 3

8 ClusterList() function 3

9 ClusterGeneList() function 3

1 Description

The MantelCorr package is based on the methodology developed in Shannon et al. [1], for which six functions are used to locate and identify important gene clusters from standard microarray expression data with \( p \) genes (rows) and \( n \) samples (columns). Mantel statistics have been applied with success to correlate gene expression levels with clinical covariates [3]. We also include a real microarray dataset with the package to help illustrate its functionality. Specifically, the package makes use of the \texttt{k-means()} function in R (with arbitrary \( k \), say \( k \in [5, \frac{p}{2}] \)) to essentially over-partition the gene space into \( k \) non-overlapping clusters. Next, two types of dissimilarity matrices are computed, one based on the original data \( D_{full} \), and one for each resultant cluster, \( D_{subset(k)} \).

Mantel [2] cluster correlations are then found by correlating each \( D_{subset(k)} \) with \( D_{full} \), resulting in \( k \) Mantel correlations. In order to destroy the distance dependent nature of \( D_{full} \) and to obtain an empirical null distribution of distance independence, a permutation test is done, where the
number of permutations and $\alpha$ significance level parameters can be chosen by the user. Specifically, the significance level provides the criterion value ($p$-value) at which a given cluster is considered significant or non-significant. Both significant and non-significant cluster lists can be viewed with the `ClusterList` function. In addition, a summary list of genes within these clusters can also be seen with the `ClusterGeneList` function.

We next introduce a simple application of the `MantelCorr` package with gene-expression training data taken from the Golub et al. [4] leukemia study.

## 2 Example R session with the Golub training data

The Golub training data consists of gene-expression values measured for 38 samples from Affymetrix Hgu6800 chips on 7,129 genes. There are 27 acute lymphoblastic leukemia (ALL) and 11 acute myeloid leukemia (AML) samples. To load the `MantelCorr` package, simply type `library(MantelCorr)`.

```r
> library(MantelCorr)
> data(GolubTrain)
> dim(GolubTrain)
[1] 7129 38
> data <- GolubTrain

## 3 Reminder

Help on any of the following `MantelCorr` package functions can be viewed by `?FunctionName`, which provides a complete description and overview of the function’s purpose and syntax. In addition, all input ‘data’ values are assumed to be interval-scale (e.g., numeric data), with gene and sample labels assigned from the `dimnames()` function.

## 4 GetClusters() function

The `GetClusters()` function over-partitions the gene-space as described in the package description. We select $k = 500$ clusters and store the result in an object called "kmeans.result".

```r
> kmeans.result <- GetClusters(data, 500, 100)
```

## 5 DistMatrices() function

A function used to compute distance matrices $D_{full}$ and $D_{subset(k)}$ from the $k$ non-overlapping clusters stored in "kmeans.result". The result is assigned to "DistMatrices.result".

```r
> DistMatrices.result <- DistMatrices(data, kmeans.result$clusters)
```
6 MantelCorrs() function

The MantelCorrs() function uses Dfull and Dsubset(k) to compute a Mantel correlation for each kth cluster by correlating these two dissimilarity matrices. The result is saved in "Mantel-Corrs.result".

> MantelCorrs.result <- MantelCorrs(DistMatrices.result$Dfull, + DistMatrices.result$Dsubsets)

7 PermutationTest() function

PermutationTest() permutes Dfull to obtain an empirical null distribution for which cluster significance is determined. We have selected 100 permutations in order to conserve CPU time, and chosen an α-value of 0.05 for the 38 Golub leukemia samples. The result is stored in an object called "permuted.pval". NOTE: we recommend using at least 1000 permutations for a thorough analysis.

> permuted.pval <- PermutationTest(DistMatrices.result$Dfull, DistMatrices.result$Dsubsets, + 100, 38, 0.05)

8 ClusterList() function

A function used to generate a complete list of both significant and non-significant clusters found by the permutation test and associated level of significance. Cluster size and correlation are provided with each type of cluster. We assign the result to the R object "ClusterLists" as follows:

> ClusterLists <- ClusterList(permuted.pval, kmeans.result$cluster.sizes, + MantelCorrs.result)

9 ClusterGeneList() function

A final function that uses information from the "ClusterList" function, coupled with the dimnames function to generate a composite list of the genes found in both cluster types (significant and non-significant). We store the result in R object "ClusterGenes".

> ClusterGenes <- ClusterGeneList(kmeans.result$clusters, ClusterLists$SignificantClusters, + data)

References

