User's Guide for Resampling Package

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1 Introduction

1.1 Objective

In order to study the effect of replicates via performing gene differential expression analyses to htseq counts data, we need to resample the original data set to construct a new truth set for a more accurate and reasonable result. Further, resampling the new truth set gives different sample subsets which can be used for subgroup comparison and analysis.

1.2 Description

Package *Resampling* provides a two-step resampling of corresponding data sets in order to generate new truth set and perform further subgroup gene differential expression analyses. It mainly consists of two parts:

- first-step resampling: rang()
- second-step resampling: card, subrang()

The first-step resampling is realized via function rang(). This function returns a sample matrix by randomly generating a desired number of sample indices for certain times from original data set. New truth sets can be constructed through this sample matrix. The second-step resampling is implemented by functions card and subrang(). card imports a sample matrix resultting from rang() and exports a list containing vectors with the information of sample partitions "liposarcoma" and "leiomyosarcoma" of the new truth sets, including

their cardinalities. Note that card is only necessary when we deal with TCGA-sarc and it has to be executed before subrang(). The other function subrang() returns an index matrix which corresponds to a group of subsets of one new truth set. These subsets can be used in further differential expression analyses.

2 Standard workflow

2.1 First-step resampling

The first-step resampling is utilized for the construction of new truth set through function rang(SEED, N, M, n). There are four parameters in rang():

- SEED: an integer used as a seed in set.seed().
- N: the number of iterations(times), positive integer.
- M: a positive integer giving the range for resampling, i.e., length of the complete set of indices of the samples. In our case, M should equals 57 for data type TCGA-luad, 100 for TCGA-brca and 162 for TCGA-sarc.
- n: a non-negative integer giving the number of indices chosen from M. n is exactly the cardinality of the new truth set if we choose TCGA-sarc, while n is half the cardinality of the new truth set if we choose TCGA-luad or TCGA-brca. rang() returns an $N \times n$ matrix that each row consists of the indices of samples in the new truth set for each iteration. Here shows the basic r code of first-step resampling.

```
library(devtools)
library(Resampling)
sam <- rang(20161220, 10, 100, 90)</pre>
```

In this example, 10 new truth sets are generated for TCGA-brca and each truth set is composed of 90 pairs of samples (180 samples). The indices of these samples are stored in matrix sam, row-wisely.

2.2 Second-step resampling

Function subrang() together with card() achieve the second-step resampling and should only be invoked after the first-step resampling because they use the result matrix of rang() as an argument. Function card() has one argument sam which corresponds to the matrix above and it returns a list comprised of four vectors:

- DL: a vector of lists giving the sample indices of "liposarcoma" in matrix sam. DL[[j]] corresponds to the jth row of sam.
- LM: a vector of lists giving the sample indices of "leiomyosarcoma" in matrix sam. LM[[j]] corresponds to the jth row of sam.
- dl: a numeric vector of the cardinalities of sample condition "liposarcoma" in matrix sam. dl[j] corresponds to the jth row of sam.
- lm: a numeric vector of the cardinalities of sample condition "leiomyosarcoma" in matrix sam. lm[j] corresponds to the jth row of sam.

Arguments involved in subrang() are listed as follows.

- SEED: an integer used as a seed in set.seed(). It differs from the value used in rang().
- N: the number of iterations(times), positive integer.
- n: a non-negative integer giving the number of indices chosen from the new truth set. Here the generated sample subset has a cardinality of 2*n. n should be no more than dim(sam)[2] for TCGA-luad or TCGA-brca. As for TCGA-sarc, since the new truth set is composed of two sample conditions: liposarcoma and leiomyosarcoma, n should not exceed the smaller cardinality of these two conditions.

- sam: matrix that is comprised of the indices of new truth sets. It's returned from rang().
- j: a positive integer giving the row index of matrix sam to choose from. j should be no larger than the number of rows of sam.
- type: character indicating the type of data, e.g., "luad", "brca", "sarc". Note that double quotes are required.

subrang() returns an $N \times n$ index matrix representing a group of subsets of one new truth set. Note that parameter j determines which new truth set obtained from rang() is involved in subrang(). Each row of the returned matrix corresponds to the generated sample subsets for each iteration. The basic steps of second-step resampling can be shown as follows.

```
library(devtools)
library(Resampling)
sam <- rang(20161220, 10, 100, 90)
samp <- subrang(20161222, 20, 5, 2, sam, "brca")</pre>
```

We use the same input in rang() as the preceding example and get sam as a 10×90 matrix. As N=20, n=5 and j=2, the new truth set is generated from the second row of sam and 20 subsets of 5 pairs of samples are constructed after the execution of subrang(). The result is stored in samp, a 20×5 matrix.

3 Examples

In this section, some examples with complete details are provided for users to get familiar with package "Resampling".

3.1 Example I

Here is the r code for the first example:

In this example, our goal is to resample the data set of TCGA-luad. First, we need to apply the first-step resampling to the original sample files to attain new truth sets. There are 57 pairs of samples, so M should be equal to 57. 100 new truth sets are generated and stored in sam, each of which consists of 50 pairs of samples. In the process of second-step resampling, 3, 5, 10, 20, 40 pairs of samples are picked from the new truth set generated by the first row of matrix sam for 50 iterations. The results are stored in samp(samp[[i]], i=1, 2, 3, 4, 5) for further analysis.

3.2 Example II

The second example is regarding the data set of TCGA-brca.

During the process of first-step resampling, 80 pairs are randomly chosen 50 times out of 100 pairs of samples to build the new truth sets. Parallel processing is performed in the second-step resampling as we pick six subsets with 3, 5, 10, 20, 50, 80 pairs of samples from the new truth set for 100 iterations. Note that under our assumptions, the new truth set is generated by the 10th row of matrix sam. The results for the second-step resampling can be found in the list samp(samp[[i]], i=1, 2, 3, 4, 5).

3.3 Example III

Finally, we shall give an example to show how to perform "resampling" to the data set of TCGA-sarc. This is slightly different from the two cases above because the numbers of "liposarcoma" and "leiomyosarcoma" are not equal and we have to figure out the exact numbers for these two conditions before resampling.

```
library(parallel)
library(Resampling)
sam <- rang(20161222, 10, 162, 140)
len <- card(sam=sam)
len$dl</pre>
```

```
## [1] 53 51 51 48 53 50 52 48 52 55
```

len\$lm

[1] 87 89 89 92 87 90 88 92 88 85

In the process of first-step resampling, parameters N and n are equal to 10 and 140, respectively. Then sam is a 10×140 matrix consisted of the new truth sets. In order to find out the partition of each truth set, we use function card on sam and save the results in len. len\$dl and len\$lm represent the numbers of samples for "liposarcoma" and "leiomyosarcoma" in each new truth set, respectively. Since len\$dl[5]=53, len\$lm[5]=87, the maximum pairs of samples we could generate from this new truth set are 53. The left can be done by following the same procedure as we did for TCGA-luad and TCGA-brca. 3, 5, 10, 20, 30, 40, 50 pairs of samples are picked from the new truth set generated by the fifth row of matrix sam for 20 iterations. The results are saved in list samp(samp[[i]], i=1, 2, 3, 4, 5, 6, 7) for further analysis.

4 Session Info

- R version 3.3.1 (2016-06-21)
- Platform: x86_64-apple-darwin13.4.0 (64-bit)
- Locale:
 - LC CTYPE=en US.UTF-8, LC NUMERIC=C
 - LC_TIME=en_US.UTF-8, LC_COLLATE=en_US.UTF-8
 - LC MONETARY=en US.UTF-8, LC MESSAGES=en US.UTF-8
- Base packages: devtools, parallel

 $footnotes^1,$

Also a quote using >:

"He who gives up [code] safety for [code] speed deserves neither." (via)

¹A footnote here.