

# Gene Set BenchMark

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## Contents

<b>1</b>	<b>Introduction</b>	<b>1</b>
<b>2</b>	<b>Datasets</b>	<b>2</b>
2.1	Pathway Data . . . . .	2
2.2	Gene Expression Datasets . . . . .	3
2.3	Matching pathway targets to gene expression datasets . . . . .	4
<b>3</b>	<b>System Information</b>	<b>6</b>
<b>4</b>	<b>Literature Cited</b>	<b>6</b>

## 1 Introduction

The GSBenchMark contains eleven expression datasets representative of different diseases. The package also contains a list of pathways and their associated gene targets. Together with these datasets and the pathways provide a benchmark for machine learning and pathway analyses, most of them used previously in [1].

## 2 Datasets

Benchmark datasets and pathway targets were downloaded from supplemental files and sources cited in [1]. These datasets covers different diseases: Leukaemia [2], Marfan [3], Melanoma [4], Prostate [5], Sarcoma [6], Head and neck cancer [7], response to breast cancer treatment [8], Bipolar disorder [9]. We also added datasets for two new diseases: Parkinson's disease [10], and Melanoma cancer[4]. We did not include two of the datasets mentioned in [1]: First, the famous Leukemia data set in [11] which is available through package `golubEsets`. Secondly, the data presented in paper [12] because the data were not available to us. These data were converted from Matlab to R for this package.

First, we load the library:

```
> require(GSBenchMark)
```

### 2.1 Pathway Data

GSBenchMark contains a list of the pathways.

```
> data(diracpathways)
> class(diracpathways)

[1] "list"

> names(diracpathways)[1:5]

[1] "DEATHPATHWAY"      "TCAPOPTOSISPATHWAY" "CCR3PATHWAY"
[4] "NEUTROPHILPATHWAY" "ALTERNATIVEPATHWAY"

> class(diracpathways[[1]])

[1] "character"

> diracpathways[[1]]

      "BID"      "TRAF2"      "TNFRSF25"      "NFKBIA"      "NFKB1"      "TNFSF12"      "CASP6"
"CASP3"      "CASP9"      "CASP7"      "BCL2"      "CASP8"      "CHUK"      "CFLAR"
"DFFA"      "DFFB"      "RELA"      "CYCS"      "LMNA"      "GAS2"      "FADD"
"BIRC4"      "BIRC3"      "BIRC2"      "TRADD"      "TNFRSF10A"      "CASP10"      "TNFSF10"
"TNFRSF10B"      "RIPK1"      "APAF1"      "MAP3K14"      "SPTAN1"

> pathways = diracpathways;
```

The variable `diracpathways` contains the pathways genes. It is a list. Each element represents a pathway with its name. Each elements contains a list of characters which represent the genes in the pathway.

## 2.2 Gene Expression Datasets

Now, we load the datasets names:

```
> data(GSBenchMarkDatasets)
> print(GSBenchMark.Dataset.names)

 [1] "leukemia_GSEA"           "marfan_GDS2960"           "melanoma_GDS2735"
 [4] "parkinsons_GDS2519"     "prostate_GDS2545_m_nf"   "prostate_GDS2545_m_p"
 [7] "prostate_GDS2545_p_nf"  "sarcoma_data"           "squamous_GDS2520"
[10] "breast_GDS807"          "bipolar_GDS2190"
```

Here is a summary of the datasets:

```
> for(i in 1: length(GSBenchMark.Dataset.names))
{
  DataSetStudy = GSBenchMark.Dataset.names[[i]]
  data(list=DataSetStudy)
  cat("Data Set ",DataSetStudy, "\n")
  print(phenotypesLevels)
  print(table(phenotypes))
}

Data Set leukemia_GSEA
  0  1
"AML" "ALL"
phenotypes
  0  1
24 24
Data Set marfan_GDS2960
  0  1
"non-MFS" "MFS"
phenotypes
  0  1
41 60
Data Set melanoma_GDS2735
  0  1
"Normal" "metastasis"
phenotypes
  0  1
23 23
Data Set parkinsons_GDS2519
  0  1
"Normal" "Parkinson's"
phenotypes
  0  1
22 50
Data Set prostate_GDS2545_m_nf
  0  1
"normal" "metastasis"
phenotypes
```

```

0 1
18 25
Data Set prostate_GDS2545_m_p
      0          1
  "primary" "metastasis"
phenotypes
0 1
65 25
Data Set prostate_GDS2545_p_nf
      0          1
  "normal" "primary"
phenotypes
0 1
18 65
Data Set sarcoma_data
      0          1
  "LMS" "GIST"
phenotypes
0 1
31 37
Data Set squamous_GDS2520
      0          1
  "Normal" "HNSCC"
phenotypes
0 1
22 22
Data Set breast_GDS807
      0          1
  "Responsive" "Non-responsive"
phenotypes
0 1
32 28
Data Set bipolar_GDS2190
      0          1
  "Normal" "Bipolar"
phenotypes
0 1
31 30

```

The data consist of three variables: `exprsdata`, `phenotypes`, and `phenotypesLevels`. `exprsdata` consists of gene expressions. `phenotypes` contains the sample labels: "0" indicates less dangerous and "1" more dangerous phenotype. `phenotypesLevels` makes the connection between "0" and "1" with the real label names e.g. "Normal" and "Parkinson's". GSBenchmark requires the rownames of gene expression variable represent the gene names, *i.e.* they are represented in the pathway information variable.

## 2.3 Matching pathway targets to gene expression datasets

One can extract the gene names by:

```

> genenames = rownames(exprsdata);
> genenames[1:10]
 [1] "DDR1" "RFC2" "HSPA6" "PAX8" "GUCA1A" "UBA7" "THRA" "PTPN21" "CCL5"
[10] "CYP2E1"

```

Also, it is possible that some of the genes in a pathway are not represented in the expression data. We prune them as the following:

```

> prunedpathways = lapply(pathways, function(x) intersect(x, genenames))
> emptypathways = which(sapply(prunedpathways, length) < 2)
> if (length(emptypathways) > 0) {
  warning(paste("After pruning the pathways, there exist pathways with zero or one genes.",
    paste(names(emptypathways), collapse = ","), "\n"))
  diracpathwayPruned= prunedpathways[-emptypathways]
}else {
  diracpathwayPruned = prunedpathways
}
> cat("Number of pathways before pruning ",length(pathways),"\n")
Number of pathways before pruning 249
> cat("Number of pathways after pruning ",length(diracpathwayPruned))
Number of pathways after pruning 249

```

phenotypes is a factor with with levels ("0","1") where "1" indicates more dangerous phenotype. For real labels, one can look at phenotypesLevels

```

> summary(phenotypes)
 0  1
31 30

> phenotypesLevels
      0      1
"Normal" "Bipolar"

```

### 3 System Information

Session information:

```
> toLatex(sessionInfo())
```

- R Under development (unstable) (2023-10-22 r85388), x86\_64-pc-linux-gnu
- Locale: LC\_CTYPE=en\_US.UTF-8, LC\_NUMERIC=C, LC\_TIME=en\_GB, LC\_COLLATE=C, LC\_MONETARY=en\_US.UTF-8, LC\_MESSAGES=en\_US.UTF-8, LC\_PAPER=en\_US.UTF-8, LC\_NAME=C, LC\_ADDRESS=C, LC\_TELEPHONE=C, LC\_MEASUREMENT=en\_US.UTF-8, LC\_IDENTIFICATION=C
- Time zone: America/New\_York
- TZcode source: system (glibc)
- Running under: Ubuntu 22.04.3 LTS
- Matrix products: default
- BLAS: /home/biocbuild/bbs-3.19-bioc/R/lib/libRblas.so
- LAPACK: /usr/lib/x86\_64-linux-gnu/lapack/liblapack.so.3.10.0
- Base packages: base, datasets, grDevices, graphics, methods, stats, utils
- Other packages: GSBenchmark 1.23.0
- Loaded via a namespace (and not attached): compiler 4.4.0, tools 4.4.0

### 4 Literature Cited

#### References

- [1] James A Eddy, Leroy Hood, Nathan D Price, and Donald Geman. Identifying tightly regulated and variably expressed networks by differential rank conservation (dirac). *PLoS computational biology*, 6(5):e1000792, 2010.
- [2] Scott A Armstrong, Jane E Staunton, Lewis B Silverman, Rob Pieters, Monique L den Boer, Mark D Minden, Stephen E Sallan, Eric S Lander, Todd R Golub, and Stanley J Korsmeyer. Mll translocations specify a distinct gene expression profile that distinguishes a unique leukemia. *Nature genetics*, 30(1):41–47, 2002.

- [3] Zizhen Yao, Jochen C Jaeger, Walter L Ruzzo, Cecile Z Morale, Mary Emond, Uta Francke, Dianna M Milewicz, Stephen M Schwartz, and Eileen R Mulvihill. A marfan syndrome gene expression phenotype in cultured skin fibroblasts. *BMC genomics*, 8(1):319, 2007.
- [4] Rebecca J Critchley-Thorne, Ning Yan, Serban Nacu, Jeffrey Weber, Susan P Holmes, and Peter P Lee. Down-regulation of the interferon signaling pathway in t lymphocytes from patients with metastatic melanoma. *PLoS Medicine*, 4(5):e176, 2007.
- [5] Uma R Chandran, Changqing Ma, Rajiv Dhir, Michelle Bisceglia, Maureen Lyons-Weiler, Wenjing Liang, George Michalopoulos, Michael Becich, and Federico A Monzon. Gene expression profiles of prostate cancer reveal involvement of multiple molecular pathways in the metastatic process. *BMC cancer*, 7(1):64, 2007.
- [6] Nathan D Price, Jonathan Trent, Adel K El-Naggar, David Cogdell, Ellen Taylor, Kelly K Hunt, Raphael E Pollock, Leroy Hood, Ilya Shmulevich, and Wei Zhang. Highly accurate two-gene classifier for differentiating gastrointestinal stromal tumors and leiomyosarcomas. *Proceedings of the National Academy of Sciences*, 104(9):3414–3419, 2007.
- [7] MA Kuriakose, WT Chen, ZM He, AG Sikora, P Zhang, ZY Zhang, WL Qiu, DF Hsu, C McMunn-Coffran, SM Brown, et al. Selection and validation of differentially expressed genes in head and neck cancer. *Cellular and Molecular Life Sciences CMLS*, 61(11):1372–1383, 2004.
- [8] Xiao-Jun Ma, Zuncai Wang, Paula D Ryan, Steven J Isakoff, Anne Barmettler, Andrew Fuller, Beth Muir, Gayatry Mohapatra, Ranelle Salunga, J Todd Tuggle, et al. A two-gene expression ratio predicts clinical outcome in breast cancer patients treated with tamoxifen. *Cancer cell*, 5(6):607–616, 2004.
- [9] MM Ryan, HE Lockstone, SJ Huffaker, MT Wayland, MJ Webster, and S Bahn. Gene expression analysis of bipolar disorder reveals downregulation of the ubiquitin cycle and alterations in synaptic genes. *Molecular psychiatry*, 11(10):965–978, 2006.
- [10] Clemens R Scherzer, Aron C Eklund, Lee J Morse, Zhixiang Liao, Joseph J Locascio, Daniel Fefer, Michael A Schwarzschild, Michael G Schlossmacher, Michael A Hauser, Jeffery M Vance, et al. Molecular markers of early parkinson’s disease based on gene expression in blood. *Proceedings of the National Academy of Sciences*, 104(3):955–960, 2007.
- [11] Todd R Golub, Donna K Slonim, Pablo Tamayo, Christine Huard, Michelle Gaasenbeek, Jill P Mesirov, Hilary Coller, Mignon L Loh, James R Downing, Mark A Caligiuri, et al. Molecular classification of cancer: class discovery and class prediction by gene expression monitoring. *science*, 286(5439):531–537, 1999.
- [12] Carlos S Moreno, Lilya Matyunina, Erin B Dickerson, Nina Schubert, Nathan J Bowen, Sanjay Logani, Benedict B Benigno, and John F McDonald. Evidence that p53-mediated cell-cycle-arrest inhibits chemotherapeutic treatment of ovarian carcinomas. *PLoS One*, 2(5):e441, 2007.