

Processed human microRNA-overexpression data from GEO, and sequence information from TargetScan, and targetScore from TargetScore

Yue Li

yueli@cs.toronto.edu

October 29, 2020

1 MicroRNA perturbation datasets

We collected 84 Gene Expression Omnibus (GEO) series corresponding to 6 platforms, 77 human cells or tissues, and 112 distinct miRNAs. To our knowledge, this is by far the largest miRNA-overexpression data compendium. To automate the data download and processing, we developed a pipeline written in R, making use of the function `getGEO` from *GEOquery* R/Bioconductor package (Davis and Meltzer [2007]). For each dataset, the pipeline downloads the raw or processed data (if available) and calculates (when necessary) the log fold-change (logFC) in treatment (miRNA transfected) vs (mock) control, taking into account the unique properties of each data. Next, we combined all of the logFC data columns into a single $N \times M$ matrix for all of the $N = 19177$ RefSeq mRNAs (NM_* obtained from UCSC) and $M = 286$ datasets. Missing data (logFC) for some genes across studies were imputed using `impute.knn` from *impute* R package (Troyanskaya et al. [2001]). For miRNA transfection data having multiple measurements (in different studies), we picked the one whose logFC correlate the most with the validated targets from mirTarBase Hsu et al. [2011] or average them if no validated target available.

```
> library(TargetScoreData)
> transfection_data <- get_miRNA_transfection_data()$transfection_data
> datasummary <-
+ list( `MicroRNA` = table(names(transfection_data)),
+       `GEO Series` = table(sapply(transfection_data, function(d)
+       `Platform` = table(sapply(transfection_data, function(df)
+       `Cell/Tissue` = table(sapply(transfection_data, function(
> print(lapply(datasummary, length))
```

```
$MicroRNA
[1] 113
```

```
$`GEO Series`
```

```
[1] 84
```

```
$Platform
```

```
[1] 6
```

```
$`Cell/Tissue`
```

```
[1] 77
```

2 TargetScan context score and PCT

TargetScan context score and PCT for all of the predicted sites (including conserved and nonconserved sites) downloaded from TargetScan website (http://www.targetscan.org/cgi-bin/targetscan/data_download.cgi?db=vert_61)

```
> targetScanCS <- get_TargetScanHuman_contextScore()  
> targetScanPCT <- get_TargetScanHuman_PCT()  
> head(targetScanCS)
```

	Gene Symbol	Transcript ID	miRNA	3prime pairing	local AU	position
1	A1CF	NM_138932	hsa-miR-4711-3p	-0.018	-0.095	-0.100
2	A1CF	NM_138933	hsa-miR-4711-3p	-0.018	-0.095	-0.100
3	A1CF	NM_014576	hsa-miR-4711-3p	-0.018	-0.095	-0.100
4	A1CF	NM_001198820	hsa-miR-4711-3p	-0.018	-0.095	-0.100
5	A1CF	NM_001198819	hsa-miR-4711-3p	-0.018	-0.095	-0.100
6	A1CF	NM_001198818	hsa-miR-4711-3p	-0.018	-0.095	-0.100

	TA	SPS	context+ score	context+ score percentile
1	0.003	0.017	-0.448	99
2	0.003	0.017	-0.448	99
3	0.003	0.017	-0.448	99
4	0.003	0.017	-0.448	99
5	0.003	0.017	-0.448	99
6	0.003	0.017	-0.448	99

```
> dim(targetScanCS)
```

```
[1] 9569357      10
```

```
> head(targetScanPCT)
```

	miR Family	Gene Symbol	Transcript ID	PCT
1	miR-22/22-3p	A1BG	NM_130786	0.00
2	miR-23abc/23b-3p	A1BG	NM_130786	0.00
7	miR-26ab/1297/4465	A1BG	NM_130786	0.00
8	miR-101/101ab	A1BG	NM_130786	0.00
9	miR-103a/107/107ab	A1BG	NM_130786	0.00
10	miR-103a/107/107ab	A1BG	NM_130786	0.09

```
> dim(targetScanPCT)
[1] 2938804      4
```

3 TargetScore

Encouraged by the superior performance of TargetScore (manuscript in peer-review), we applied TargetScore to all of the transfection data above. For further exploring miRNA targetome and their associations, we enclose the targetScores results in this package.

```
> targetScoreMatrix <- get_precomputed_targetScores()
> head(names(targetScoreMatrix))

[1] "hsa-miR-34b" "hsa-miR-34c" "hsa-miR-205" "hsa-miR-124" "hsa-miR-1"
[6] "hsa-miR-181a"

> head(targetScoreMatrix[[1]])

           logFC targetScanCS targetScanPCT targetScore
SGIP1      0.077526011          0.00           0  0.03489650
AGBL4      0.020639084          0.00           0  0.03388637
NECAP2     0.078650400          0.00           0  0.03492518
CLIC4      0.016043400         -0.03           0  0.24335149
ADC        -0.002303429          0.00           0  0.03417828
SLC45A1   -0.018655797          0.00           0  0.03457975
```

We can reproduce targetScores using the above data as demonstrated in the following example (require *TargetScore* package). As a convenience function, we applied a wrapper function called `getTargetScores` that does the following: (1) given a miRNA ID, obtain fold-change(s) from `logFC.imputed` matrix or use the user-supplied fold-changes; (2) retrieves TargetScan context score (CS) and PCT (if found); (3) obtain validated targets from the local `mirTarBase` file; (4) compute `targetScore`. We apply `getTargetScores` function using miRNA `hsa-miR-1`, which we know has all three types of data, namely `logFC`, `targetScan` context score, and `PCT`.

```
> library(TargetScore)
> library(gplots)
> myTargetScores <- getTargetScores("hsa-miR-1", tol=1e-3, maxiter=200)
> table((myTargetScores$targetScore > 0.1), myTargetScores$validated) # a v
> # obtain all of targetScore for all of the 112 miRNA
>
> logFC.imputed <- get_precomputed_logFC()
> mirIDs <- unique(colnames(logFC.imputed))
>
> # takes time
>
> # targetScoreMatrix <- mclapply(mirIDs, getTargetScores)
>
> # names(targetScoreMatrix) <- mirIDs
```

4 Session Info

```
> sessionInfo()
```

```
R version 4.0.3 (2020-10-10)  
Platform: x86_64-pc-linux-gnu (64-bit)  
Running under: Ubuntu 18.04.5 LTS
```

```
Matrix products: default  
BLAS: /home/biocbuild/bbs-3.12-bioc/R/lib/libRblas.so  
LAPACK: /home/biocbuild/bbs-3.12-bioc/R/lib/libRlapack.so
```

```
locale:  
 [1] LC_CTYPE=en_US.UTF-8      LC_NUMERIC=C  
 [3] LC_TIME=en_US.UTF-8      LC_COLLATE=C  
 [5] LC_MONETARY=en_US.UTF-8  LC_MESSAGES=en_US.UTF-8  
 [7] LC_PAPER=en_US.UTF-8     LC_NAME=C  
 [9] LC_ADDRESS=C             LC_TELEPHONE=C  
[11] LC_MEASUREMENT=en_US.UTF-8 LC_IDENTIFICATION=C
```

```
attached base packages:  
[1] stats      graphics  grDevices  utils      datasets  methods    base
```

```
other attached packages:  
[1] TargetScoreData_1.26.0
```

```
loaded via a namespace (and not attached):  
[1] compiler_4.0.3 tools_4.0.3
```

References

- Sean Davis and Paul S Meltzer. GEOquery: a bridge between the Gene Expression Omnibus (GEO) and BioConductor. *Bioinformatics (Oxford, England)*, 23(14):1846–1847, July 2007.
- Sheng-Da Hsu, Feng-Mao Lin, Wei-Yun Wu, Chao Liang, Wei-Chih Huang, Wen-Ling Chan, Wen-Ting Tsai, Goun-Zhou Chen, Chia-Jung Lee, Chih-Min Chiu, Chia-Hung Chien, Ming-Chia Wu, Chi-Ying Huang, Ann-Ping Tsou, and Hsien-Da Huang. miRTarBase: a database curates experimentally validated microRNA-target interactions. *Nucleic acids research*, 39 (Database issue):D163–9, January 2011.
- O Troyanskaya, M Cantor, G Sherlock, P Brown, T Hastie, R Tibshirani, D Botstein, and R B Altman. Missing value estimation methods for DNA microarrays. *Bioinformatics (Oxford, England)*, 17(6):520–525, June 2001.