Supplementary Tables

Selcen Ari Yuka

Alper Yilmaz

2019-12-27

Table S1: *minsamp* sample dataset that includes interaction factors. The parameters which affect miRNA:target interactions (i.e. seed type, region, energy) are provided in sample dataset.

competing	miRNA	Competing_expression	$miRNA_expression$	seed_type	region	energy
Gene1	Mir1	10000	1000	0.43	0.30	-20
Gene2	Mir1	10000	1000	0.43	0.01	-15
Gene3	Mir1	5000	1000	0.32	0.40	-14
Gene4	Mir1	10000	1000	0.23	0.50	-10
Gene4	Mir2	10000	2000	0.35	0.90	-12
Gene5	Mir2	5000	2000	0.05	0.40	-11
Gene6	Mir2	10000	2000	0.01	0.80	-25

Table S2: Efficiency factors for seed types.

	seed_type	seed_ty	pe_effect
1	6-mer_noncanonical		0.05
2	9-mer		0.43
3	6-mer		0.07
4	8-mer		0.43
5	7-mer		0.23
6	none		0.01
7	5-mer_noncanonical		0.04
8	5-mer		0.05
9	6-merA1_noncanonical		0.05
10	7-mer-8m_noncanonical		0.21
11	7-mer- 8 m		0.25
12	8-mer_noncanonical		0.35
13	7-merA1_noncanonical		0.16
14	7-merA1		0.19
15	6-merA1		0.07

Some of information about miRNA:target interactions were exhibited directly by high-throughput studies. On the other haned, we were examined other interaction factors based on different studies.

- Helwak et al. (2013) and Moore et al.(- Moore et al. 2015) reported the energy values in miRNA:target interactions.
- Comparisons of canonical seed types were evaluated by study of Grimson et al. (2007), while functional and non-functional seed interactions were studied by Bartel et al. (2009) and Betel et al. (2010) (Table S2).

Table S3: Efficiency factors for binding regions on targets

	region	region	effect
		1081011_	
1	3UTR		0.84
2	CDS		0.42
3	3UTRCDS		0.93
4	5UTR		0.01
5	5UTRCDS		0.42
6	none		0.01
7	intron		0.01
8	CDS3UTR		0.93
9	CDS5UTR		0.42
10	$exon_unclassified$		0.20
11	CDS3UTRintron		0.93
12	3UTRintron		0.84
13	CDSintron		0.42
14	5UTRintron		0.01
15	5UTR 3 UTR		0.93
16	CDS5UTR3UTR		0.93

• Numeric definition of target region location effect was performed based on studies of Hausser et al. (2013) and Helwak et al. (2013) (Table S3).

Table S4: Example of E9GE_mirnagenenormal dataset. Hugo Symbol, gene symbol; miRNA name, name of miRNA that interacted with specified gene; mirna RPM; mirna count in read per million; seed type and region effect, numeric seed type and region coefficients for specified miRNA:gene interactions based on Table S2 and S3.

Hugo Symbol	miRNA name	mirna RPM	GE normal	energy	seed type effect	region effect
ENAH	hsa-let-7a-5p	111204.15	7540	-22.70	0.01	0.00
GALNT2	hsa-let-7a-5p	111204.15	2824	-20.50	0.14	0.00
RLF	hsa-let-7a-5p	111204.15	1144	-18.00	0.03	0.20
MAST2	hsa-let-7a-5p	111204.15	2640	-22.60	0.24	0.00
DOCK1	hsa-let-7a-5p	111204.15	4826	-20.50	0.01	0.00
ZBTB16	hsa-let-7a-5p	111204.15	315	-24.30	0.14	0.00

Table S5: Context of miRNA:target pairs dataset supported by High-throughput Experiments

Variable	Structure	Means
cluster	character	Barcode from experimentally method
chromosome	character	Chromosome of Target gene from raw data
start_position	numeric	Gene start position from raw data
end_position	numeric	Gene end position from raw data
strand	character	Gene strand
hgnc_symbol	character	Gene name (Symbol)
Ensembl_Gene_Id	character	Ensembl Gene Id of gene
Ensembl_Transcript_Id	character	Ensembl transcript id of mRNA of Target gene
$target_seq$	character	mRNA sequences targeted by miRNA
miRNA	character	miRNA id (from miRBase version 21)
miR_seq	character	miRNA sequence
$\operatorname{seed_type}$	character	seed type of miRNA:target interaction
Energy	numeric	Energy of miRNA:target binding
HG38build_loc	character	Recent chromosomal location of Gene
Genome_build	character	Genome build of given chromosome, start and end positions
region	character	interaction location on target
$region_effect$	numeric	Coefficient of location on target
seed_type_effect	numeric	Coefficient for seed sequence of miRNA:target interaction

As a result of simulation a dataset, a graph object is obtained that includes various variables in edge and node data. A graph object includes variables at following.

Table S6: The context of graph object during the process.

Variables	Structure	Means
Node Variables		
name	character	node name
type	character	Competing or miRNA
$\operatorname{node_id}$	numeric	in on graph object
$initial_count$	numeric	Initial Expression value of node
count _pre	numeric	Expression value of node at previous regulation
count_current	numeric	Existing expression value of node
$changes_variable$	character	Regulation of node (Up, down or steady)
Edge Variables		
Competing name	character	name of genes
miRNA name	character	name of miRNAs
Competing expression	numeric	Expression values of competing elements at steady-state
miRNA expression	numeric	Expression values of miRNA elements at steady-state
energy	numeric	coefficient of miRNA:target interactions (binding affinity)
seed type	numeric	coefficient of miRNA:target interactions (binding affinity)
region	$\operatorname{numeric}$	coefficient of miRNA:target interactions (degradation efficiency)
afff factor	$\operatorname{numeric}$	coefficient scaled and combined affinity factor
degg factor	$\operatorname{numeric}$	coefficient scaled and combined degradation factor
$comp_count_list$	list	list of competing expression for each iteration
$comp_count$	numeric	pre: competing expression at previous iteration; current: competing
		expression at present iteration
$mirna_count_list$	list	list of miRNA expression for each iteration
$mirna_count$	$\operatorname{numeric}$	pre: miRNA expression at previous iteration; current: miRNA ex-
		pression at present iteration
effect	numeric	pre: total miRNA reppressive effect on individual target at previous
		iteration ; current: miRNA reppressive effect on individual target at
		present iteration
$effect_list$	list	list of miRNA reppressive effect on individual target for each itera-
		tion

REFERENCES

Bartel, David P. 2009. "MicroRNAs: Target Recognition and Regulatory Functions." Cell 136 (2): 215–33. https://doi.org/10.1016/j.cell.2009.01.002.

Betel, Doron, Anjali Koppal, Phaedra Agius, Chris Sander, and Christina Leslie. 2010. "Comprehensive Modeling of microRNA Targets Predicts Functional Non-Conserved and Non-Canonical Sites." *Genome Biology* 11 (8): R90.

Grimson, Andrew, Kyle Kai-How Farh, Wendy K. Johnston, Philip Garrett-Engele, Lee P. Lim, and David P. Bartel. 2007. "MicroRNA Targeting Specificity in Mammals: Determinants Beyond Seed Pairing." *Molecular Cell* 27 (1): 91–105. https://doi.org/10.1016/j.molcel.2007.06.017.

Hausser, J., A. P. Syed, B. Bilen, and M. Zavolan. 2013. "Analysis of CDS-Located miRNA Target Sites Suggests That They Can Effectively Inhibit Translation." *Genome Research* 23 (4): 604–15. https://doi.org/10.1101/gr.139758.112.

Helwak, Aleksandra, Grzegorz Kudla, Tatiana Dudnakova, and David Tollervey. 2013. "Mapping the Human miRNA Interactome by CLASH Reveals Frequent Noncanonical Binding." *Cell* 153 (3): 654–65. https://doi.org/10.1016/j.cell.2013.03.043.

Moore, Michael J., Troels K. H. Scheel, Joseph M. Luna, Christopher Y. Park, John J. Fak, Eiko Nishiuchi, Charles M. Rice, and Robert B. Darnell. 2015. "miRNA-Target Chimeras Reveal miRNA 3'-End Pairing

as a Major Determinant of Argonaute Target Specificity." $Nature\ Communications\ 6$ (November): 8864. https://doi.org/10.1038/ncomms9864.