

Package ‘KBoost’

July 20, 2025

Type Package

Title Inference of gene regulatory networks from gene expression data

Version 1.16.0

Description Reconstructing gene regulatory networks and transcription factor activity is crucial to understand biological processes and holds potential for developing personalized treatment. Yet, it is still an open problem as state-of-art algorithm are often not able to handle large amounts of data. Furthermore, many of the present methods predict numerous false positives and are unable to integrate other sources of information such as previously known interactions. Here we introduce KBoost, an algorithm that uses kernel PCA regression, boosting and Bayesian model averaging for fast and accurate reconstruction of gene regulatory networks. KBoost can also use a prior network built on previously known transcription factor targets. We have benchmarked KBoost using three different datasets against other high performing algorithms. The results show that our method compares favourably to other methods across datasets.

Depends R (>= 4.1), stats, utils

License GPL-2 | GPL-3

Encoding UTF-8

LazyData true

RoxygenNote 7.1.1

URL <https://github.com/Luisiglm/KBoost>

biocViews Network, GraphAndNetwork, Bayesian, NetworkInference, GeneRegulation, Transcriptomics, SystemsBiology, Transcription, GeneExpression, Regression, PrincipalComponent

Suggests knitr, rmarkdown, testthat

VignetteBuilder knitr

git_url <https://git.bioconductor.org/packages/KBoost>

git_branch RELEASE_3_21

git_last_commit fe6e4e7

git_last_commit_date 2025-04-15

Repository Bioconductor 3.21

Date/Publication 2025-07-20

Author Luis F. Iglesias-Martinez [aut, cre] (ORCID:
<https://orcid.org/0000-0002-9110-2189>),
 Barbara de Kegel [aut],
 Walter Kolch [aut]

Maintainer Luis F. Iglesias-Martinez <luis.iglesiasmartinez@ucd.ie>

Contents

add_names	3
AUPR_AUROC_matrix	3
d4_mfac	4
D4_multi_1	5
D4_multi_2	5
D4_multi_3	6
D4_multi_4	7
D4_multi_5	7
Gerstein_Prior_ENET_2	8
get_prior_Gerstein	8
get_tfs_human	9
grid_search_kboost	10
G_D4_multi_1	10
G_D4_multi_2	11
G_D4_multi_3	12
G_D4_multi_4	12
G_D4_multi_5	13
Human_TFs	14
irma_check	14
IRMA_Gold	15
irma_off	15
irma_on	16
kboost	17
KBoost_human_symbol	17
kernel_normal	18
kernel_pc_boosting	19
KPC	19
net_dist_bin	20
net_refine	21
net_summary_bin	21
RBF_K	22
tab_2_matrix_D4	23
write_GRN_D4	23

Index

25

add_names	<i>Function to add names to network for the user.</i>
-----------	---

Description

Function to add names to network for the user.

Usage

```
add_names(grn, gen_names)
```

Arguments

grn	a GRN object from KBoost.
gen_names	a vector with the gene names.

Value

grn a GRN object with elements with user-defined gene names.

Examples

```
data(D4_multi_1)
Net = kboost(D4_multi_1)
g_names = matrix("G",100,1)
for (i in seq_along(g_names)){
  g_names[i] = paste(g_names[i],toString(i), sep = "")
}
Net = add_names(Net,g_names)
```

AUPR_AUROC_matrix	<i>Function to calculate the AUROC and AUPR of a known network. This function was made to test the R implementation of the KBoost Package.</i>
-------------------	--

Description

Function to calculate the AUROC and AUPR of a known network. This function was made to test the R implementation of the KBoost Package.

Usage

```
AUPR_AUROC_matrix(Net, G_mat, auto_remove, TFs, upper_limit)
```

Arguments

Net	An inferred gene regulatory network
G_mat	A matrix with the gold standard network.
auto_remove	TRUE if the auto-regulation is to be discarded.
TFs	the indexes of the rows of Net that are TFs.
upper_limit	Top number of edges to use.

Value

list object with AUPR and AUROC of gold standard in matrix format.

Examples

```
data(D4_multi_1)
Net = kboost(D4_multi_1)
g_mat1 = tab_2_matrix_D4(KBoost::G_D4_multi_1,100)
aupr_auroc = AUPR_AUROC_matrix(Net$GRN,g_mat1,auto_remove = TRUE, seq_len(100))
```

d4_mfac	<i>Function to obtain the AUPR and AUROC in the DREAM4 Multifactorial Challenge.</i>
---------	--

Description

Function to obtain the AUPR and AUROC in the DREAM4 Multifactorial Challenge.

Usage

```
d4_mfac(v, g, ite, write_res)
```

Arguments

v	a number between 0 and 1 that is the shrinkage parameter
g	a number larger than 0, width parameter for the RBF Kernel
ite	an integer with number of iterations.
write_res	a logical to indicate if the tables should be written.

Value

list with auroc and auprs of the DREAM4 multifactorial challenge.

Examples

```
res = d4_mfac()
```

D4_multi_1*Dream 4 multifactorial pertubation challenge dataset 1*

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
D4_multi_1
```

Format

```
matrix
```

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(D4_multi_1)
```

D4_multi_2*Dream 4 multifactorial pertubation challenge dataset 2*

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
D4_multi_2
```

Format

```
matrix
```

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(D4_multi_2)
```

D4_multi_3

Dream 4 multifactorial perturbation challenge dataset 3

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
D4_multi_3
```

Format

matrix

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(D4_multi_3)
```

D4_multi_4*Dream 4 multifactorial pertubation challenge dataset 4*

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
D4_multi_4
```

Format

```
matrix
```

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(D4_multi_4)
```

D4_multi_5*Dream 4 multifactorial pertubation challenge dataset 5*

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
D4_multi_5
```

Format

```
matrix
```

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(D4_multi_5)
```

Gerstein_Prior_ENET_2 *Gene Regulatory Network from human ChIP-Seq data in Encode*

Description

A gene regulatory network inferred from the ChIP-Seq Encode dataset Table with two columns
The first column is a transcription factor and the second is a gene.

Usage

```
Gerstein_Prior_ENET_2
```

Format

```
matrix
```

References

Gerstein, M.B., et al. Architecture of the human regulatory network derived from ENCODE data. Nature 2012;489(7414):91-100.

Examples

```
data(Gerstein_Prior_ENET_2)
```

get_prior_Gerstein *Function to build a prior using a previously built Network on ChIP-Seq.*

Description

Function to build a prior using a previously built Network on ChIP-Seq.

Usage

```
get_prior_Gerstein(gen_names, TFs, pos_weight, neg_weight)
```

Arguments

gen_names	the gene names in Symbol nomenclature.
Tfs	the indexes of gene names which are TFs.
pos_weight	the prior weight for edges previously found in Gerstein 2011
neg_weight	the prior weight for edges not found in the Gerstein 2011/

Value

matrix with prior probabilities of the Tf target edges.

Examples

```
gen_names = c("TP53", "MDM2", "FOXO1", "ESR1", "CTCF", "YY1")
tfs = get_tfs_human(gen_names)
prior = get_prior_Gerstein(gen_names, tfs, 0.6, 0.4)
```

get_tfs_human	<i>Function to automatically assign Human TFs given a list of Symbols.</i>
---------------	--

Description

Function to automatically assign Human TFs given a list of Symbols.

Usage

```
get_tfs_human(gen_names)
```

Arguments

gen_names	a vector or matrix with the Symbol Gene Names of the system.
-----------	--

Value

indexes of gen_names who are TFs.

Examples

```
gen_names = c("TP53", "MDM2", "FOXO1", "ESR1", "CTCF")
tfs = get_tfs_human(gen_names)
```

grid_search_kboost	<i>Function to perform a grid search and find the hyperparameters.</i>
--------------------	--

Description

Function to perform a grid search and find the hyperparameters.

Usage

```
grid_search_kboost(dataset, vs, gs, ite)
```

Arguments

dataset	1 for IRMA or 2 for DREAM4 multifactorial.
vs	The range of values of v. All values need to be between 0 and 1.
gs	The range of values of g. All values need to be larger than 0.
ite	An integer that is the number of iterations, fixed in this case.

Value

list with auprs and aurops of different values of vs and gs and ite.

Examples

```
res = grid_search_kboost(1,c(0.1,0.5,1),c(1,10,60,100),3)
```

G_D4_multi_1	<i>Gold Standard Dream 4 multifactorial pertubation challenge dataset 1</i>
--------------	---

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
G_D4_multi_1
```

Format

matrix

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(G_D4_multi_1)
```

G_D4_multi_2	<i>Gold Standard Dream 4 multifactorial pertubation challenge dataset</i>
	2

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
G_D4_multi_2
```

Format

matrix

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(G_D4_multi_2)
```

G_D4_multi_3	<i>Gold Standard Dream 4 multifactorial pertubation challenge dataset</i> 3
--------------	--

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
G_D4_multi_3
```

Format

```
matrix
```

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(G_D4_multi_3)
```

G_D4_multi_4	<i>Gold Standard Dream 4 multifactorial pertubation challenge dataset</i> 4
--------------	--

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
G_D4_multi_4
```

Format

```
matrix
```

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(G_D4_multi_4)
```

G_D4_multi_5	<i>Gold Standard Dream 4 multifactorial pertubation challenge dataset</i>
	5

Description

Each column is a gene and each row is a simulated experiment.

Usage

```
G_D4_multi_5
```

Format

```
matrix
```

Source

<https://www.synapse.org/#!Synapse:syn3049712/wiki/74628>

References

Marbach D, Prill RJ, Schaffter T, Mattiussi C, Floreano D, and Stolovitzky G. Revealing strengths and weaknesses of methods for gene network inference. PNAS, 107(14):6286-6291, 2010. Pubmed

Examples

```
data(G_D4_multi_5)
```

Human_TFs	<i>Index of human genes' Symbols, Entrez and Ensembl for K-Boost Pacakge that correspond to transcription factors.</i>
-----------	--

Description

Table with three columns corresponding to Symbol

Usage

Human_TFs

Format

matrix

References

Lambert, S.A., et al. The Human Transcription Factors. Cell 2018;172(4):650-665.

Examples

data(Human_TFs)

irma_check	<i>Function to produce the AUPR and AUROC Results on the IRMA datasets.</i>
------------	---

Description

Function to produce the AUPR and AUROC Results on the IRMA datasets.

Usage

irma_check(v, g, ite)

Arguments

v	a number between 0 and 1 that is the shrinkage parameter
g	a number larger than 0 that is the width parameter for the RBF Kernel
ite	an integer with number of iterations.

Value

list with aurocs and auprs for IRMA datasets

Examples

```
res = irma_check()
```

IRMA_Gold*IRMA Gold Standard Network*

Description

Matrix where the rows are genes and columns are transcription factor.

Usage

```
IRMA_Gold
```

Format

```
matrix
```

Source

<https://www.sciencedirect.com/science/article/pii/S0092867409001561>

References

Cantone, I., et al. A Yeast Synthetic Network for In Vivo Assessment of Reverse-Engineering and Modeling Approaches. Cell 2009;137(1):172-181.

Examples

```
data(IRMA_Gold)
```

irma_off*IRMA Off Dataset*

Description

Matrix where the rows are experiments and columns are genes for the IRMA Off dataset.

Usage

```
irma_off
```

Format

```
matrix
```

Source

<https://www.sciencedirect.com/science/article/pii/S0092867409001561>

References

Cantone, I., et al. A Yeast Synthetic Network for In Vivo Assessment of Reverse-Engineering and Modeling Approaches. Cell 2009;137(1):172-181.

Examples

```
data(irma_off)
```

irma_on

IRMA On Dataset

Description

Matrix where the rows are experiments and columns are genes for the IRMA Off dataset.

Usage

```
irma_on
```

Format

```
matrix
```

Source

<https://www.sciencedirect.com/science/article/pii/S0092867409001561>

References

Cantone, I., et al. A Yeast Synthetic Network for In Vivo Assessment of Reverse-Engineering and Modeling Approaches. Cell 2009;137(1):172-181.

Examples

```
data(irma_on)
```

kboost	<i>A function to run KBoost.</i>
--------	----------------------------------

Description

A function to run KBoost.

Usage

```
kboost(X, TFs, g, v, prior_weights, ite)
```

Arguments

X	an NxG matrix with the expression values of G genes and N obsvs..
TFs	a Kx1 numeric matrix with integers of columns of X that are TFs.
g	a positive no., width parameter for RBF kernel. (default g = 40)
v	a no. between 0 and 1 with the shrinkage parameter. (default v =0.1)
prior_weights	it can be a scalar or GxK. (default 0.5)
ite	an integer for the maximum number of iterations (default 3)

Value

a list with the results for kboost, with fields: GRN a matrix with the posterior edge probability after network refinement. GRN_UP a matrix with the posterior edges before refinement. model a matrix with logical values for the TFs selected for each gene. g the width parameter for the RBF kernel. v the shrinkage parameter. prior the prior of each model. TFs a matrix with integers of each gene that is a TF. prior_weights the prior_weights with which KBoost was run. run_time a scalar with the running time.

Examples

```
data(D4_multi_1)
Net <- kboost(D4_multi_1)
```

KBoost_human_symbol	<i>Function for KBoost on data from a human sample annotated with Symbol names.</i>
---------------------	---

Description

Function for KBoost on data from a human sample annotated with Symbol names.

Usage

```
KBoost_human_symbol(X, gen_names, g, v, ite, pos_weight, neg_weight)
```

Arguments

X	an NxG matrix with the expression values of G genes and N samples.
gen_names	SYMBOL gene names corresponding to the columns of X.
g	a positive no., width parameter for the RBF kernel. (default g = 40)
v	a double between 0 and 1, the shrinkage parameter. (default v = 0.1)
ite	an integer with the number of iterations (default ite = 3)
pos_weight	no. between 0 and 1. Prior that a TF regulate a gene.
neg_weight	no. between 0 and 1, for TF gene pairs not seen before.

Value

list with results of KBoost on a dataset with Symbol gene names.

Examples

```
X = rnorm(50,0,1)
X = matrix(X,10,5)
gen_names = c("TP53", "YY1", "CTCF", "MDM2", "ESR1")
grn = KBoost_human_symbol(X, gen_names, pos_weight = 0.6, neg_weight = 0.4)
```

kernel_normal	<i>A function to perform feature normalization in kernel space.</i>
---------------	---

Description

A function to perform feature normalization in kernel space.

Usage

```
kernel_normal(K)
```

Arguments

K	an NxN numeric matrix with the kernel function with N observations.
---	---

Value

feature centred kernel.

Examples

```
x = rnorm(100,0,1)
k = RBF_K(x,40)
k_ = kernel_normal(k)
```

kernel_pc_boosting	<i>Function to perform Kernel Principal Component Boosting</i>
--------------------	--

Description

Function to perform Kernel Principal Component Boosting

Usage

```
kernel_pc_boosting(X, Y, g, v, ite, thr)
```

Arguments

X	A matrix with the explanatory variables.
Y	a matrix with the variable to predict.
g	a positive number with the width parameter for the RBF Kernel.
v	a number between 0 and 1 that corresponds to the shrinkage parameter.
ite	an integer with the number of iterations.
thr	a threshold to discard Kernel principal components whose eigenvalue

Value

function an sum of squared errors.

Examples

```
data(D4_multi_1)
Y = scale(matrix(D4_multi_1[,91],100,1))
X = scale(D4_multi_1[, -91])
res = kernel_pc_boosting(X,Y, g= 40, v = 0.5, ite = 3, thr = 1e-10)
```

KPC	<i>Function to calculate the principal components of a kernel.</i>
-----	--

Description

Function to calculate the principal components of a kernel.

Usage

```
KPC(K, thr)
```

Arguments

K	an NxN numeric matrix with the Kernel matrix.
thr	a positive scalar which is a threshold to discard eigen-vectors based on eigen-values.

Value

the kernel principal components

Examples

```
x = rnorm(100,0,1)
k = RBF_K(x,1)
k_ = kernel_normal(k)
kpca = KPC(k,1e-8)
```

net_dist_bin	<i>Function to calculate the distance between nodes.</i>
--------------	--

Description

Function to calculate the distance between nodes.

Usage

```
net_dist_bin(GRN, TFs, thr)
```

Arguments

GRN	An inferred networks with the predictive probabilities that a transcription factor regulates a gene.
TFs	A vector with indexes of the rows of GRN which correspond to TFs.
thr	A scalar between 0 and 1 that is used select the edges with large posterior probabilities.

Value

a matrix with the distances between edges.

Examples

```
data(D4_multi_1)
Net = kboost(D4_multi_1)
dist = net_dist_bin(Net$GRN,Net$TFs,0.1)
```

net_refine	<i>Function to do a heuristic post-processing that improves accuracy. Each column is multiplied by its variance.</i>
------------	--

Description

Function to do a heuristic post-processing that improves accuracy. Each column is multiplied by its variance.

Usage

```
net_refine(Net)
```

Arguments

Net	a GRN with TFs in the columns.
-----	--------------------------------

Value

the network with Slavek and Arodz heuristic

Examples

```
Net = rbeta(10000, 1, 2)
Net = matrix(Net, 100, 100)
net_ref = net_refine(Net)
```

net_summary_bin	<i>Function to summarize the GRN filtered with a threshold,</i>
-----------------	---

Description

Function to summarize the GRN filtered with a threshold,

Usage

```
net_summary_bin(GRN, TFs, thr, a, b)
```

Arguments

GRN	An inferred network
TFs	A vector with indexes of the rows of GRN which correspond to TFs.
thr	a scalar between 0 and 1, a threshold for posterior probabilities.
a	parameter for Katz and PageRank centrality (default the inverse of the largest eigenvalue of GRN).
b	parameter for Katz and PageRank centrality (default b = 1).

Value

list with table version of the GRN, outdegree and indegree, and closeness centrality.

Examples

```
data(D4_multi_1)
Net = kboost(D4_multi_1)
Net_Summary = net_summary_bin(Net$GRN)
```

RBF_K	<i>Function to calculate the RBF Kernel of a matrix X with width g.</i>
-------	---

Description

Function to calculate the RBF Kernel of a matrix X with width g.

Usage

```
RBF_K(x, g)
```

Arguments

- x an Nx1 numeric matrix with N observations.
- g a positive scalar with the width parameter.

Value

the matrix with the RBF kernel

Examples

```
x = rnorm(100,0,1)
k = RBF_K(x,40)
```

tab_2_matrix_D4	<i>Function to produce the gold standard of the DREAM4 Multifactorial Challenge in matrix format.</i>
-----------------	---

Description

Function to produce the gold standard of the DREAM4 Multifactorial Challenge in matrix format.

Usage

```
tab_2_matrix_D4(g_table, G)
```

Arguments

g_table	the network in table format. The first column is the Tf, the second column the gene, and the third indicates if there is an interaction.
G	the number of genes.

Value

a network in table format transformed into a matrix.

Examples

```
g_table = KBoost::G_D4_multi_1
g_mat = tab_2_matrix_D4(g_table,100)
```

write_GRN_D4	<i>Function to write output in DREAM4 Challenge Format.</i>
--------------	---

Description

Function to write output in DREAM4 Challenge Format.

Usage

```
write_GRN_D4(GRN, TFs, filename)
```

Arguments

GRN	a GxK gene regulatory network.
TFs	a K set of indexes of G that are TFs.
filename	a string with the filename.

Value

a file with the network written as a file.

Examples

```
data(D4_multi_1)
Net = kboost(D4_multi_1)
write_GRN_D4(Net$GRN, seq_len(100), "D4_multi_1_network.txt")
```

Index

* datasets

- D4_multi_1, [5](#)
- D4_multi_2, [5](#)
- D4_multi_3, [6](#)
- D4_multi_4, [7](#)
- D4_multi_5, [7](#)
- G_D4_multi_1, [10](#)
- G_D4_multi_2, [11](#)
- G_D4_multi_3, [12](#)
- G_D4_multi_4, [12](#)
- G_D4_multi_5, [13](#)
- Gerstein_Prior_ENET_2, [8](#)
- Human_TFs, [14](#)
- IRMA_Gold, [15](#)
- irma_off, [15](#)
- irma_on, [16](#)

[add_names](#), [3](#)

[AUPR_AUROC_matrix](#), [3](#)

[d4_mfac](#), [4](#)

- D4_multi_1, [5](#)
- D4_multi_2, [5](#)
- D4_multi_3, [6](#)
- D4_multi_4, [7](#)
- D4_multi_5, [7](#)

- G_D4_multi_1, [10](#)
- G_D4_multi_2, [11](#)
- G_D4_multi_3, [12](#)
- G_D4_multi_4, [12](#)
- G_D4_multi_5, [13](#)

[Gerstein_Prior_ENET_2](#), [8](#)

[get_prior_Gerstein](#), [8](#)

[get_tfs_human](#), [9](#)

[grid_search_kboost](#), [10](#)

[Human_TFs](#), [14](#)

[irma_check](#), [14](#)

[IRMA_Gold](#), [15](#)

[irma_off](#), [15](#)

[irma_on](#), [16](#)

[kboost](#), [17](#)

[KBoost_human_symbol](#), [17](#)

[kernel_normal](#), [18](#)

[kernel_pc_boosting](#), [19](#)

[KPC](#), [19](#)

[net_dist_bin](#), [20](#)

[net_refine](#), [21](#)

[net_summary_bin](#), [21](#)

[RBF_K](#), [22](#)

[tab_2_matrix_D4](#), [23](#)

[write_GRN_D4](#), [23](#)