BoolNet Inference (E-GEOD-18494)

Expression profiling of hypoxic HepG2 hepatoma, U87 glioma, and MDA-MB231 breast cancer cells: time course (E-GEOD-18494)

Analysis of expression changes of cultured HepG2 hepatoma, U87 glioma, and MDA-MB231 breast cancer cells subjected to hypoxia (0.5% O2) for 0, 4, 8, 12 hours . Results provide insight to cell type-specific response to hypoxia. HepG2 hepatoma, U87 glioma, and MDA-MB231 breast cancer cells were collected under normoxic conditions (~19% O2, 0 hours) and after 4, 8 and 12 hours of hypoxia treatment (0.5% O2). For each cell line, three replicates of total RNA at each time point were prepared using Trizol and submitted to the DFCI Microarray Core for labeling, hybridization to Affymetrix HG-U133Plus2 oligonucleotide arrays and image scanning.

https://www.ebi.ac.uk/arrayexpress/experiments/E-GEOD-18494/

```
packages_cran = c("igraph", "BoolNet", "BiocManager", "tidyverse", "fs")


# Install and load packages
package.check <- lapply(packages_cran, FUN = function(x) {
  if (!require(x, character.only = TRUE)) {
    install.packages(x, dependencies = TRUE)
    library(x, character.only = TRUE)
  }
})

library(RSQLite, lib.loc = "/usr/local/lib/R/site-library")

# For oligo and ArrayExpress First install:
#install.packages('https://cran.r-project.org/src/contrib/Archive/ff/ff_2.2-14.tar.gz',repos=NULL)

packages_bioconductor = c("Biobase", "GEOquery", "ArrayExpress", "hgu133plus2.db", "preprocessCore")

# Install and load packages
package.check <- lapply(packages_bioconductor, FUN = function(x) {
  if (!require(x, character.only = TRUE)) {
    BiocManager::install(x, dependencies = TRUE)
    library(x, character.only = TRUE)
  }
})

rm(package.check, packages_bioconductor, packages_cran)
```

```
download_dir <- fs::path(".data_tmp")
if (!dir_exists(download_dir)) {
    dir_create(download_dir)
    EGEOD18494 <- ArrayExpress( "E-GEOD-18494", save=TRUE, path=download_dir)
} else {
```

```
    EGEOD18494 <- ArrayExpress( "E-GEOD-18494", save=TRUE, path=download_dir)
}
```

```
## Reading in : .data_tmp/GSM460679.CEL
## Reading in : .data_tmp/GSM460699.CEL
## Reading in : .data_tmp/GSM460681.CEL
## Reading in : .data_tmp/GSM460685.CEL
## Reading in : .data_tmp/GSM460700.CEL
## Reading in : .data_tmp/GSM460675.CEL
## Reading in : .data_tmp/GSM460695.CEL
## Reading in : .data_tmp/GSM460686.CEL
## Reading in : .data_tmp/GSM460677.CEL
## Reading in : .data_tmp/GSM460698.CEL
## Reading in : .data_tmp/GSM460678.CEL
## Reading in : .data_tmp/GSM460696.CEL
## Reading in : .data_tmp/GSM460697.CEL
## Reading in : .data_tmp/GSM460693.CEL
## Reading in : .data_tmp/GSM460692.CEL
## Reading in : .data_tmp/GSM460683.CEL
## Reading in : .data_tmp/GSM460676.CEL
## Reading in : .data_tmp/GSM460673.CEL
## Reading in : .data_tmp/GSM460690.CEL
## Reading in : .data_tmp/GSM460684.CEL
## Reading in : .data_tmp/GSM460688.CEL
## Reading in : .data_tmp/GSM460687.CEL
## Reading in : .data_tmp/GSM460669.CEL
## Reading in : .data_tmp/GSM460682.CEL
## Reading in : .data_tmp/GSM460671.CEL
## Reading in : .data_tmp/GSM460702.CEL
## Reading in : .data_tmp/GSM460701.CEL
## Reading in : .data_tmp/GSM460674.CEL
## Reading in : .data_tmp/GSM460691.CEL
## Reading in : .data_tmp/GSM460704.CEL
## Reading in : .data_tmp/GSM460680.CEL
## Reading in : .data_tmp/GSM460670.CEL
## Reading in : .data_tmp/GSM460694.CEL
## Reading in : .data_tmp/GSM460672.CEL
## Reading in : .data_tmp/GSM460703.CEL
## Reading in : .data_tmp/GSM460689.CEL
```

```
data.EGEOD18494 <- Biobase::pData(EGEOD18494)

data.EGEOD18494 <- data.frame(
                  codes = substr(data.EGEOD18494$Source.Name,1,9),
                  cell_line = data.EGEOD18494$Characteristics..cell.line.,
                  time = data.EGEOD18494$Characteristics..time,
                  condition = data.EGEOD18494$Characteristics..stress.
                  )
data.EGEOD18494 <- data.EGEOD18494[order(data.EGEOD18494$codes),]
data.EGEOD18494$rep <- rep(1:3, n= length(data.EGEOD18494$codes))

# Normalisation
eset.EGEOD18494 <- oligo::rma(EGEOD18494,  normalize = TRUE)
```

```
## Background correcting
## Normalizing
## Calculating Expression
```

```
exp.EGEOD18494 <- exprs(eset.EGEOD18494)

colnames(exp.EGEOD18494) <- substr(colnames(exp.EGEOD18494),1,9)

EGEOD18494@annotation
```

```
## [1] "pd.hg.u133.plus.2"
```

```
rm(download_dir)
```

Convert the probes to Symbol names

```
anno.EGEOD18494 <- AnnotationDbi::select(hgu133plus2.db, keys=rownames(exp.EGEOD18494), columns=c("ENSE
```

```
## 'select()' returned 1:many mapping between keys and columns
```

```
colnames(anno.EGEOD18494) <- c("probes", "ensgene", "symbol", "description")
```

Selecting the HIF Genes

```
# Selecting genes from HIF Axis
hif.symbols <- c("TP53", "HIF1A", "EP300", "MDM2", "VHL")

hif.probes <- anno.EGEOD18494$probes[anno.EGEOD18494$symbol %in% hif.symbols]

# Select the probes and genes
exp.EGEOD18494.hif <- as.data.frame(exp.EGEOD18494) %>%
  rownames_to_column('probes') %>%
  filter(probes %in% hif.probes) %>%
  merge(anno.EGEOD18494[anno.EGEOD18494$symbol %in% hif.symbols, c("probes","symbol")], by = "probes") %
  #distinct(symbol, .keep_all = TRUE) %>% # Take the first one
  dplyr::select(!(probes))


# Function to binarize according an consensus mean of probes, add the O2 state and rename columns
binNet <- function(b){
  binarizeTimeSeries(b[,-5], method="kmeans")$binarizedMeasurements  %>%
  as.data.frame(.)  %>%
  aggregate(., list(symbol = b$symbol), mean) %>%
  mutate_at(vars(-symbol), funs(ifelse(. > 0.4, 1, 0))) %>%
  rbind(., c("O2", 1,0,0,0)) %>%
    rename_at(vars(data.EGEOD18494$codes[data.EGEOD18494$codes %in% names(b)] ),
```

```
            ~paste0(substr(data.EGEOD18494$condition[data.EGEOD18494$codes %in% names(b)],1,4),".",
                    data.EGEOD18494$time[data.EGEOD18494$codes %in% names(b)],".",
                    substr(data.EGEOD18494$cell_line[data.EGEOD18494$codes %in% names(b)],1,1), ".",
                    data.EGEOD18494$rep[data.EGEOD18494$codes %in% names(b)])) %>%
  column_to_rownames("symbol")
}
```

Exemplifying the Binarization

```
breast1x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "MDA-MB231 breast cancer" &
                  data.EGEOD18494$rep == 1], "symbol")) %>% arrange(symbol)

names(breast1x) <- c("norm.control.M.1",  "hypo.4h.M.1", "hypo.8h.M.1", "hypo.12h.M.1", "symbol")

breast1x[, c("symbol","norm.control.M.1",  "hypo.4h.M.1", "hypo.8h.M.1", "hypo.12h.M.1")]
```

```
##    symbol norm.control.M.1 hypo.4h.M.1 hypo.8h.M.1 hypo.12h.M.1
## 1   EP300         7.117723    7.444650    7.564863     7.102371
## 2   EP300         7.413672    7.507501    7.570583     7.374402
## 3   HIF1A        12.201881   11.633014   10.456373    10.119609
## 4    MDM2         5.524042    5.320023    5.350573     5.446186
## 5    MDM2         4.045154    3.853332    4.078569     4.257243
## 6    MDM2         5.078994    4.927372    5.029658     4.981994
## 7    MDM2         6.355831    6.328876    6.389927     6.806724
## 8    MDM2         4.287158    4.755383    4.670058     4.462138
## 9    MDM2         8.162994    8.179121    8.219938     8.085525
## 10   MDM2         7.285900    7.207761    7.123573     6.955918
## 11   MDM2         3.623543    3.829355    3.753720     4.100483
## 12   MDM2         4.054654    4.129631    4.067410     4.256327
## 13   MDM2         8.207312    7.778604    7.656600     7.797764
## 14   TP53         8.895355    8.773830    9.104009     9.136858
## 15   TP53         8.600345    8.240598    8.641253     8.664151
## 16    VHL         7.698038    7.713089    7.348580     7.098092
## 17    VHL         3.738962    3.749649    3.759698     3.638137
```

```
binarizeTimeSeries(breast1x[,-5], method="kmeans")$binarizedMeasurements  %>%
  as.data.frame(.)  %>%
  add_column(symbol = breast1x$symbol) %>%   dplyr::select( c("symbol","norm.control.M.1",  "hypo.4h.M.
```

```
##    symbol norm.control.M.1 hypo.4h.M.1 hypo.8h.M.1 hypo.12h.M.1
## 1   EP300               0           1           1            0
## 2   EP300               0           1           1            0
## 3   HIF1A               1           1           0            0
## 4    MDM2               1           0           0            1
## 5    MDM2               1           0           1            1
## 6    MDM2               1           0           1            0
## 7    MDM2               0           0           0            1
## 8    MDM2               0           1           1            0
```

```
## 9    MDM2                1           1           1           0
## 10   MDM2                1           1           1           0
## 11   MDM2                0           0           0           1
## 12   MDM2                0           0           0           1
## 13   MDM2                1           0           0           0
## 14   TP53                0           0           1           1
## 15   TP53                1           0           1           1
## 16    VHL                1           1           0           0
## 17    VHL                1           1           1           0
```

```
binarizeTimeSeries(breast1x[,-5], method="kmeans")$binarizedMeasurements  %>%
  as.data.frame(.)  %>%
  aggregate(., list(symbol = breast1x$symbol), mean) %>%
  mutate_at(vars(-symbol), funs(ifelse(. > 0.4, 1, 0))) %>%
  rbind(., c("O2", 1,0,0,0))
```

```
## Warning: `funs()` is deprecated as of dplyr 0.8.0.
## Please use a list of either functions or lambdas:
##
##   # Simple named list:
##   list(mean = mean, median = median)
##
##   # Auto named with `tibble::lst()`:
##   tibble::lst(mean, median)
##
##   # Using lambdas
##   list(~ mean(., trim = .2), ~ median(., na.rm = TRUE))
## This warning is displayed once every 8 hours.
## Call `lifecycle::last_warnings()` to see where this warning was generated.
```

```
##   symbol norm.control.M.1 hypo.4h.M.1 hypo.8h.M.1 hypo.12h.M.1
## 1  EP300                0           1           1            0
## 2  HIF1A                1           1           0            0
## 3   MDM2                1           0           1            1
## 4   TP53                1           0           1            1
## 5    VHL                1           1           1            0
## 6     O2                1           0           0            0
```

MDA-MB231 breast cancer

```
breast1x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "MDA-MB231 breast cancer" &
                  data.EGEOD18494$rep == 1], "symbol"))  %>%
  binNet(.)
breast1x
```

```
##       norm.control.M.1 hypo.4h.M.1 hypo.8h.M.1 hypo.12h.M.1
## EP300                0           1           1            0
## HIF1A                1           1           0            0
```

```
## MDM2                 1           0           1           1
## TP53                 1           0           1           1
## VHL                  1           1           1           0
## O2                   1           0           0           0
```

```
breast2x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "MDA-MB231 breast cancer" &
                  data.EGEOD18494$rep == 2], "symbol"))  %>%
  binNet(.)
breast2x
```

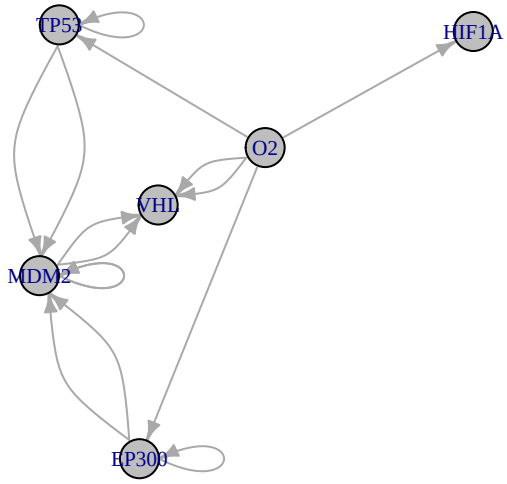
```
##       norm.control.M.2 hypo.4h.M.2 hypo.8h.M.2 hypo.12h.M.2
## EP300                1           0           1            1
## HIF1A                1           1           0            0
## MDM2                 1           0           1            0
## TP53                 0           1           1            1
## VHL                  1           1           1            0
## O2                   1           0           0            0
```

```
breast3x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "MDA-MB231 breast cancer" &
                  data.EGEOD18494$rep == 3], "symbol"))  %>%
  binNet(.)
breast3x
```

```
##       norm.control.M.3 hypo.4h.M.3 hypo.8h.M.3 hypo.12h.M.3
## EP300                0           1           1            1
## HIF1A                1           1           0            0
## MDM2                 1           1           0            1
## TP53                 0           1           1            1
## VHL                  1           1           0            1
## O2                   1           0           0            0
```

```
# All breast cancer nets merged:

net <- reconstructNetwork(list(breast1x, breast2x, breast3x), method="bestfit",returnPBN=TRUE,readableF
plotNetworkWiring(net)
```



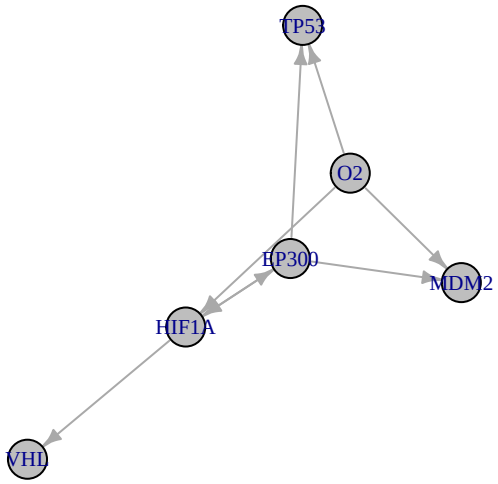

```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (!O2) | (!EP300) ( probability: 1, error: 1)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (O2) ( probability: 1, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (!MDM2 & TP53) | (!EP300 & MDM2 & !TP53) | (EP300 & !MDM2) ( probability: 0.5, error: 1)
## MDM2 = (!MDM2) | (!EP300 & !TP53) ( probability: 0.5, error: 1)
##
## Alternative transition functions for gene TP53:
## TP53 = (!O2) | (!TP53) ( probability: 1, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (!MDM2 & !O2) | (MDM2 & O2) ( probability: 0.5, error: 0)
## VHL = (!MDM2) | (O2) ( probability: 0.5, error: 0)
```

```
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## O2 = 0
```

```
# Individual nets of each replica:

net <- reconstructNetwork(breast1x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```

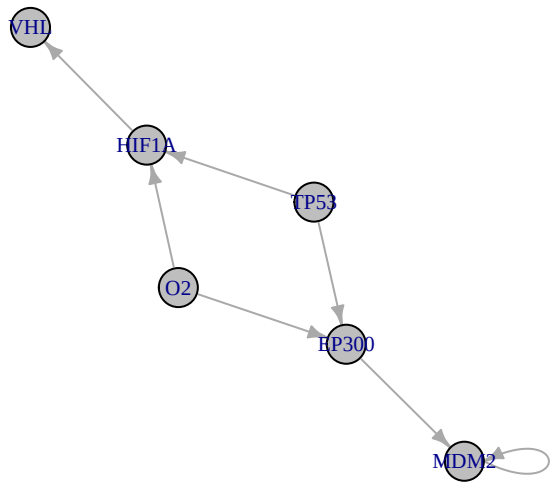



```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (HIF1A) ( probability: 1, error: 0)
##
## Alternative transition functions for gene HIF1A:
```

```
## HIF1A = (O2) ( probability: 0.5, error: 0)
## HIF1A = (!EP300) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (!O2) ( probability: 0.5, error: 0)
## MDM2 = (EP300) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = (!O2) ( probability: 0.5, error: 0)
## TP53 = (EP300) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (HIF1A) ( probability: 1, error: 0)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## O2 = 0
```

```
net <- reconstructNetwork(breast2x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```

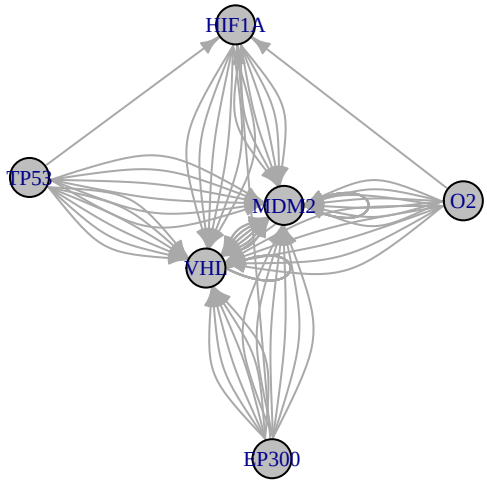



```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
```

```
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (!O2) ( probability: 0.5, error: 0)
## EP300 = (TP53) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (O2) ( probability: 0.5, error: 0)
## HIF1A = (!TP53) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (!MDM2) ( probability: 0.5, error: 0)
## MDM2 = (!EP300) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = 1 ( probability: 1, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (HIF1A) ( probability: 1, error: 0)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## TP53 = 1
## O2 = 0
```

```
net <- reconstructNetwork(breast3x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```




```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = 1 ( probability: 1, error: 0)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (O2) ( probability: 0.3333333, error: 0)
## HIF1A = (!TP53) ( probability: 0.3333333, error: 0)
## HIF1A = (!EP300) ( probability: 0.3333333, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (!VHL & !O2) | (VHL & O2) ( probability: 0.05555556, error: 0)
## MDM2 = (!VHL) | (O2) ( probability: 0.05555556, error: 0)
## MDM2 = (!TP53 & VHL) | (TP53 & !VHL) ( probability: 0.05555556, error: 0)
## MDM2 = (!VHL) | (!TP53) ( probability: 0.05555556, error: 0)
## MDM2 = (!MDM2 & !O2) | (MDM2 & O2) ( probability: 0.05555556, error: 0)
## MDM2 = (!MDM2) | (O2) ( probability: 0.05555556, error: 0)
## MDM2 = (!MDM2 & TP53) | (MDM2 & !TP53) ( probability: 0.05555556, error: 0)
```

```
## MDM2 = (!TP53) | (!MDM2) ( probability: 0.05555556, error: 0)
## MDM2 = (!HIF1A & !O2) | (HIF1A & O2) ( probability: 0.05555556, error: 0)
## MDM2 = (!HIF1A) | (O2) ( probability: 0.05555556, error: 0)
## MDM2 = (!HIF1A & TP53) | (HIF1A & !TP53) ( probability: 0.05555556, error: 0)
## MDM2 = (!TP53) | (!HIF1A) ( probability: 0.05555556, error: 0)
## MDM2 = (!EP300 & VHL) | (EP300 & !VHL) ( probability: 0.05555556, error: 0)
## MDM2 = (!VHL) | (!EP300) ( probability: 0.05555556, error: 0)
## MDM2 = (!EP300 & MDM2) | (EP300 & !MDM2) ( probability: 0.05555556, error: 0)
## MDM2 = (!MDM2) | (!EP300) ( probability: 0.05555556, error: 0)
## MDM2 = (!EP300 & HIF1A) | (EP300 & !HIF1A) ( probability: 0.05555556, error: 0)
## MDM2 = (!HIF1A) | (!EP300) ( probability: 0.05555556, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = 1 ( probability: 1, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (!VHL & !O2) | (VHL & O2) ( probability: 0.05555556, error: 0)
## VHL = (!VHL) | (O2) ( probability: 0.05555556, error: 0)
## VHL = (!TP53 & VHL) | (TP53 & !VHL) ( probability: 0.05555556, error: 0)
## VHL = (!VHL) | (!TP53) ( probability: 0.05555556, error: 0)
## VHL = (!MDM2 & !O2) | (MDM2 & O2) ( probability: 0.05555556, error: 0)
## VHL = (!MDM2) | (O2) ( probability: 0.05555556, error: 0)
## VHL = (!MDM2 & TP53) | (MDM2 & !TP53) ( probability: 0.05555556, error: 0)
## VHL = (!TP53) | (!MDM2) ( probability: 0.05555556, error: 0)
## VHL = (!HIF1A & !O2) | (HIF1A & O2) ( probability: 0.05555556, error: 0)
## VHL = (!HIF1A) | (O2) ( probability: 0.05555556, error: 0)
## VHL = (!HIF1A & TP53) | (HIF1A & !TP53) ( probability: 0.05555556, error: 0)
## VHL = (!TP53) | (!HIF1A) ( probability: 0.05555556, error: 0)
## VHL = (!EP300 & VHL) | (EP300 & !VHL) ( probability: 0.05555556, error: 0)
## VHL = (!VHL) | (!EP300) ( probability: 0.05555556, error: 0)
## VHL = (!EP300 & MDM2) | (EP300 & !MDM2) ( probability: 0.05555556, error: 0)
## VHL = (!MDM2) | (!EP300) ( probability: 0.05555556, error: 0)
## VHL = (!EP300 & HIF1A) | (EP300 & !HIF1A) ( probability: 0.05555556, error: 0)
## VHL = (!HIF1A) | (!EP300) ( probability: 0.05555556, error: 0)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## EP300 = 1
## TP53 = 1
## O2 = 0
```

HepG2 hepatoma

```
hepatoma1x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "HepG2 hepatoma" &
                  data.EGEOD18494$rep == 1], "symbol"))  %>%
  binNet(.)
hepatoma1x
```

```
##       norm.control.H.1 hypo.4h.H.1 hypo.8h.H.1 hypo.12h.H.1
## EP300                1           1           0             0
## HIF1A                0           0           1             0
## MDM2                 1           1           0             1
## TP53                 1           1           0             1
## VHL                  1           0           1             0
## O2                   1           0           0             0
```

```
hepatoma2x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "HepG2 hepatoma" &
                  data.EGEOD18494$rep == 2], "symbol"))  %>%
  binNet(.)
hepatoma2x
```

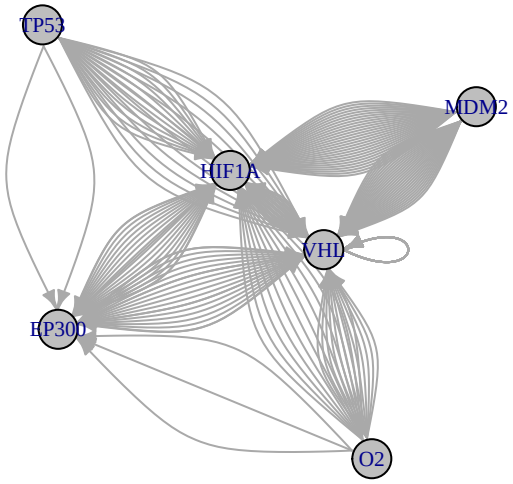
```
##       norm.control.H.2 hypo.4h.H.2 hypo.8h.H.2 hypo.12h.H.2
## EP300                0           1           1             1
## HIF1A                0           0           1             0
## MDM2                 0           1           1             1
## TP53                 0           1           1             0
## VHL                  1           0           1             1
## O2                   1           0           0             0
```

```
hepatoma3x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "HepG2 hepatoma" &
                  data.EGEOD18494$rep == 3], "symbol"))  %>%
  binNet(.)
hepatoma3x
```

```
##       norm.control.H.3 hypo.4h.H.3 hypo.8h.H.3 hypo.12h.H.3
## EP300                1           1           0             1
## HIF1A                0           1           1             0
## MDM2                 0           1           0             1
## TP53                 1           1           1             1
## VHL                  1           1           0             0
## O2                   1           0           0             0
```

```
# All nets hepatoma merged:

net <- reconstructNetwork(list(hepatoma1x, hepatoma2x, hepatoma3x), method="bestfit",returnPBN=TRUE,rea
plotNetworkWiring(net)
```




```
print(net)
```

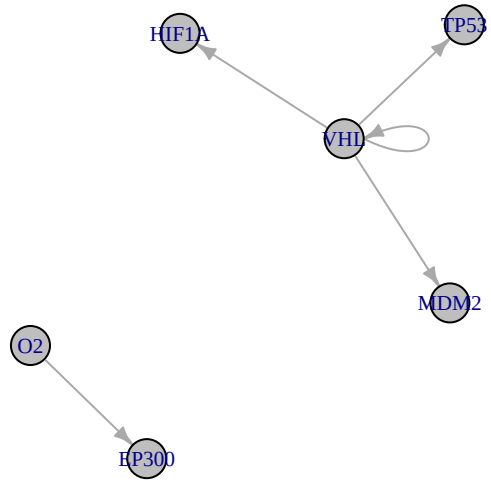
```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (!VHL & !O2) | (VHL & O2) ( probability: 0.1666667, error: 2)
## EP300 = (!VHL) | (O2) ( probability: 0.1666667, error: 2)
## EP300 = (O2) | (TP53) ( probability: 0.1666667, error: 2)
## EP300 = (!HIF1A & VHL) | (HIF1A & !VHL) ( probability: 0.1666667, error: 2)
## EP300 = (!VHL) | (!HIF1A) ( probability: 0.1666667, error: 2)
## EP300 = (!HIF1A) | (TP53) ( probability: 0.1666667, error: 2)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (!MDM2 & TP53 & O2) | (MDM2 & TP53 & !O2) ( probability: 0.03571429, error: 1)
## HIF1A = (!MDM2 & TP53 & O2) | (MDM2 & !TP53 & O2) | (MDM2 & TP53 & !O2) ( probability: 0.03571429, e
## HIF1A = (!MDM2 & TP53 & O2) | (MDM2 & !O2) ( probability: 0.03571429, error: 1)
## HIF1A = (!MDM2 & TP53 & O2) | (MDM2 & !O2) | (MDM2 & !TP53) ( probability: 0.03571429, error: 1)
## HIF1A = (!MDM2 & TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.03571429, error: 1)
## HIF1A = (!MDM2 & TP53 & VHL) | (MDM2 & !TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.03571429
## HIF1A = (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) ( probability: 0.03571429, error: 1)
```

```
## HIF1A = (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) | (MDM2 & !TP53) ( probability: 0.03571429, error: 1)
## HIF1A = (!MDM2 & !TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.035714
## HIF1A = (!MDM2 & !TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !TP53 & VHL) | (MDM2 & TP53 & !VHL)
## HIF1A = (!TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) ( probability: 0.03571429, error: 1)
## HIF1A = (!TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !TP53) | (MDM2 & !VHL) ( probability: 0.0357
## HIF1A = (EP300 & !MDM2 & O2) | (EP300 & MDM2 & !O2) ( probability: 0.03571429, error: 1)
## HIF1A = (EP300 & !O2) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## HIF1A = (!EP300 & MDM2 & O2) | (EP300 & !MDM2 & O2) | (EP300 & MDM2 & !O2) ( probability: 0.03571429
## HIF1A = (!EP300 & MDM2 & O2) | (EP300 & !O2) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## HIF1A = (MDM2 & !O2) | (EP300 & !MDM2 & O2) ( probability: 0.03571429, error: 1)
## HIF1A = (MDM2 & !O2) | (EP300 & !O2) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## HIF1A = (MDM2 & !O2) | (!EP300 & MDM2) | (EP300 & !MDM2 & O2) ( probability: 0.03571429, error: 1)
## HIF1A = (MDM2 & !O2) | (!EP300 & MDM2) | (EP300 & !O2) | (EP300 & !MDM2) ( probability: 0.03571429, e
## HIF1A = (EP300 & !MDM2 & VHL) | (EP300 & MDM2 & !VHL) ( probability: 0.03571429, error: 1)
## HIF1A = (EP300 & !VHL) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## HIF1A = (!EP300 & MDM2 & VHL) | (EP300 & !MDM2 & VHL) | (EP300 & MDM2 & !VHL) ( probability: 0.035714
## HIF1A = (!EP300 & MDM2 & VHL) | (EP300 & !VHL) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## HIF1A = (MDM2 & !VHL) | (EP300 & !MDM2 & VHL) ( probability: 0.03571429, error: 1)
## HIF1A = (MDM2 & !VHL) | (EP300 & !VHL) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## HIF1A = (MDM2 & !VHL) | (!EP300 & MDM2) | (EP300 & !MDM2 & VHL) ( probability: 0.03571429, error: 1)
## HIF1A = (MDM2 & !VHL) | (!EP300 & MDM2) | (EP300 & !VHL) | (EP300 & !MDM2) ( probability: 0.03571429
##
## Alternative transition functions for gene MDM2:
## MDM2 = 1 ( probability: 1, error: 2)
##
## Alternative transition functions for gene TP53:
## TP53 = 1 ( probability: 1, error: 2)
##
## Alternative transition functions for gene VHL:
## VHL = (!MDM2 & TP53 & O2) | (MDM2 & TP53 & !O2) ( probability: 0.03571429, error: 1)
## VHL = (!MDM2 & TP53 & O2) | (MDM2 & !TP53 & O2) | (MDM2 & TP53 & !O2) ( probability: 0.03571429, erro
## VHL = (!MDM2 & TP53 & O2) | (MDM2 & !O2) ( probability: 0.03571429, error: 1)
## VHL = (!MDM2 & TP53 & O2) | (MDM2 & !O2) | (MDM2 & !TP53) ( probability: 0.03571429, error: 1)
## VHL = (!MDM2 & TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.03571429, error: 1)
## VHL = (!MDM2 & TP53 & VHL) | (MDM2 & !TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.03571429, e
## VHL = (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) ( probability: 0.03571429, error: 1)
## VHL = (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) | (MDM2 & !TP53) ( probability: 0.03571429, error: 1)
## VHL = (!MDM2 & !TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.03571429
## VHL = (!MDM2 & !TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !TP53 & VHL) | (MDM2 & TP53 & !VHL) ( p
## VHL = (!TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) ( probability: 0.03571429, error: 1)
## VHL = (!TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !TP53) | (MDM2 & !VHL) ( probability: 0.035714
## VHL = (EP300 & !MDM2 & O2) | (EP300 & MDM2 & !O2) ( probability: 0.03571429, error: 1)
## VHL = (EP300 & !O2) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## VHL = (!EP300 & MDM2 & O2) | (EP300 & !MDM2 & O2) | (EP300 & MDM2 & !O2) ( probability: 0.03571429, e
## VHL = (!EP300 & MDM2 & O2) | (EP300 & !O2) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## VHL = (MDM2 & !O2) | (EP300 & !MDM2 & O2) ( probability: 0.03571429, error: 1)
## VHL = (MDM2 & !O2) | (EP300 & !O2) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## VHL = (MDM2 & !O2) | (!EP300 & MDM2) | (EP300 & !MDM2 & O2) ( probability: 0.03571429, error: 1)
## VHL = (MDM2 & !O2) | (!EP300 & MDM2) | (EP300 & !O2) | (EP300 & !MDM2) ( probability: 0.03571429, er
## VHL = (EP300 & !MDM2 & VHL) | (EP300 & MDM2 & !VHL) ( probability: 0.03571429, error: 1)
## VHL = (EP300 & !VHL) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## VHL = (!EP300 & MDM2 & VHL) | (EP300 & !MDM2 & VHL) | (EP300 & MDM2 & !VHL) ( probability: 0.0357142
## VHL = (!EP300 & MDM2 & VHL) | (EP300 & !VHL) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## VHL = (MDM2 & !VHL) | (EP300 & !MDM2 & VHL) ( probability: 0.03571429, error: 1)
```

```
## VHL = (MDM2 & !VHL) | (EP300 & !VHL) | (EP300 & !MDM2) ( probability: 0.03571429, error: 1)
## VHL = (MDM2 & !VHL) | (!EP300 & MDM2) | (EP300 & !MDM2 & VHL) ( probability: 0.03571429, error: 1)
## VHL = (MDM2 & !VHL) | (!EP300 & MDM2) | (EP300 & !VHL) | (EP300 & !MDM2) ( probability: 0.03571429, e
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## MDM2 = 1
## TP53 = 1
## O2 = 0
```

```
# Individual nets of each replica:

net <- reconstructNetwork(hepatoma1x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```

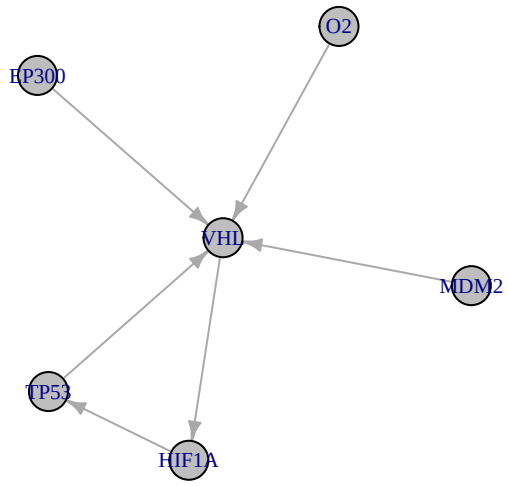



```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
```

```
##
## Alternative transition functions for gene EP300:
## EP300 = (O2) ( probability: 1, error: 0)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (!VHL) ( probability: 1, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (VHL) ( probability: 1, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = (VHL) ( probability: 1, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (!VHL) ( probability: 1, error: 0)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## O2 = 0
```

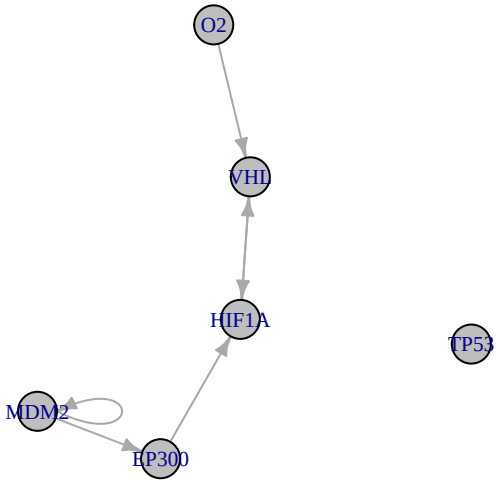
```
net <- reconstructNetwork(hepatoma2x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```



```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = 1 ( probability: 1, error: 0)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (!VHL) ( probability: 1, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = 1 ( probability: 1, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = (!HIF1A) ( probability: 1, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (!O2) ( probability: 0.25, error: 0)
## VHL = (TP53) ( probability: 0.25, error: 0)
## VHL = (MDM2) ( probability: 0.25, error: 0)
## VHL = (EP300) ( probability: 0.25, error: 0)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## EP300 = 1
## MDM2 = 1
## O2 = 0
```

```
net <- reconstructNetwork(hepatoma3x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```




```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (!MDM2) ( probability: 1, error: 0)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (VHL) ( probability: 0.5, error: 0)
## HIF1A = (EP300) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (!MDM2) ( probability: 1, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = 1 ( probability: 1, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (O2) ( probability: 0.5, error: 0)
## VHL = (!HIF1A) ( probability: 0.5, error: 0)
```

```
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## TP53 = 1
## O2 = 0
```

U87 glioma

```
glioma1x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "U87 glioma" &
                  data.EGEOD18494$rep == 1], "symbol"))  %>%
  binNet(.)
glioma1x
```

```
##       norm.control.U.1 hypo.4h.U.1 hypo.8h.U.1 hypo.12h.U.1
## EP300                1           0           0            1
## HIF1A                1           0           0            0
## MDM2                 1           0           0            0
## TP53                 1           0           1            1
## VHL                  1           1           0            1
## O2                   1           0           0            0
```

```
glioma2x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "U87 glioma" &
                  data.EGEOD18494$rep == 2], "symbol"))  %>%
  binNet(.)
glioma2x
```

```
##       norm.control.U.2 hypo.4h.U.2 hypo.8h.U.2 hypo.12h.U.2
## EP300                1           0           1            0
## HIF1A                1           1           0            0
## MDM2                 0           0           0            1
## TP53                 1           0           1            0
## VHL                  0           1           1            0
## O2                   1           0           0            0
```

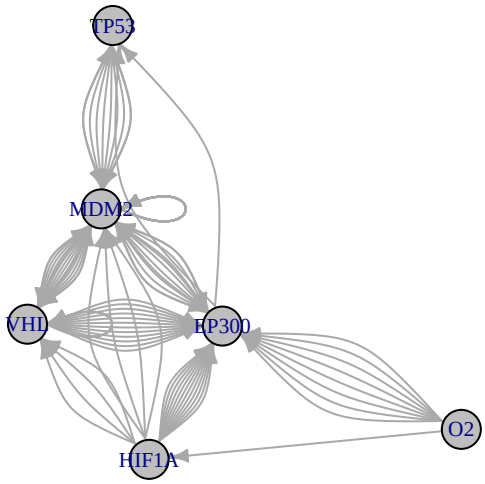
```
glioma3x <-
exp.EGEOD18494.hif %>%
  dplyr::select(c(data.EGEOD18494$codes[data.EGEOD18494$cell_line == "U87 glioma" &
                  data.EGEOD18494$rep == 3], "symbol"))  %>%
  binNet(.)
glioma3x
```

```
##       norm.control.U.3 hypo.4h.U.3 hypo.8h.U.3 hypo.12h.U.3
## EP300                1           1           1            0
```

```
## HIF1A                1          1          0          0
## MDM2                 1          1          1          0
## TP53                 1          1          1          1
## VHL                  1          0          1          1
## O2                   1          0          0          0
```

```
# All glioma nets merged:

net <- reconstructNetwork(list(glioma1x, glioma2x, glioma3x), method="bestfit",returnPBN=TRUE,readableF
plotNetworkWiring(net)
```



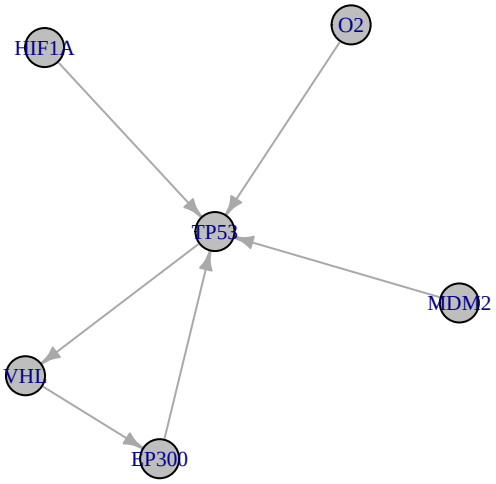

```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (!VHL & !O2) | (HIF1A & !O2) ( probability: 0.08333333, error: 1)
## EP300 = (!VHL & !O2) | (HIF1A & !O2) | (HIF1A & VHL) ( probability: 0.08333333, error: 1)
## EP300 = (!VHL & !O2) | (!HIF1A & VHL & O2) | (HIF1A & !O2) ( probability: 0.08333333, error: 1)
## EP300 = (!VHL & !O2) | (VHL & O2) | (HIF1A & !O2) ( probability: 0.08333333, error: 1)
```

```
## EP300 = (!VHL & !O2) | (!HIF1A & !VHL) | (HIF1A & !O2) ( probability: 0.08333333, error: 1)
## EP300 = (!VHL & !O2) | (!HIF1A & !VHL) | (HIF1A & !O2) | (HIF1A & VHL) ( probability: 0.08333333, er
## EP300 = (!VHL & !O2) | (!HIF1A & O2) | (HIF1A & !O2) ( probability: 0.08333333, error: 1)
## EP300 = (!VHL & !O2) | (!HIF1A & O2) | (HIF1A & !O2) | (VHL & O2) ( probability: 0.08333333, error:
## EP300 = (!HIF1A & !MDM2 & !VHL) | (HIF1A & !MDM2 & VHL) | (HIF1A & MDM2 & !VHL) ( probability: 0.083
## EP300 = (!HIF1A & !MDM2 & !VHL) | (HIF1A & VHL) | (HIF1A & MDM2) ( probability: 0.08333333, error: 1
## EP300 = (!HIF1A & !VHL) | (HIF1A & !MDM2 & VHL) | (MDM2 & !VHL) ( probability: 0.08333333, error: 1)
## EP300 = (!HIF1A & !VHL) | (HIF1A & VHL) | (MDM2 & !VHL) ( probability: 0.08333333, error: 1)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (O2) ( probability: 1, error: 1)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (!MDM2 & TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.0625, error: 1)
## MDM2 = (!MDM2 & TP53 & VHL) | (MDM2 & !TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.0625, err
## MDM2 = (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) ( probability: 0.0625, error: 1)
## MDM2 = (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) | (MDM2 & !TP53) ( probability: 0.0625, error: 1)
## MDM2 = (!MDM2 & !TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & TP53 & !VHL) ( probability: 0.0625, e
## MDM2 = (!MDM2 & !TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !TP53 & VHL) | (MDM2 & TP53 & !VHL) (
## MDM2 = (!TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !VHL) ( probability: 0.0625, error: 1)
## MDM2 = (!TP53 & !VHL) | (!MDM2 & TP53 & VHL) | (MDM2 & !TP53) | (MDM2 & !VHL) ( probability: 0.0625,
## MDM2 = (EP300 & !MDM2 & VHL) | (EP300 & MDM2 & !VHL) ( probability: 0.0625, error: 1)
## MDM2 = (!EP300 & MDM2 & VHL) | (EP300 & !MDM2 & VHL) | (EP300 & MDM2 & !VHL) ( probability: 0.0625,
## MDM2 = (MDM2 & !VHL) | (EP300 & !MDM2 & VHL) ( probability: 0.0625, error: 1)
## MDM2 = (MDM2 & !VHL) | (!EP300 & MDM2) | (EP300 & !MDM2 & VHL) ( probability: 0.0625, error: 1)
## MDM2 = (EP300 & !HIF1A & !MDM2) | (EP300 & HIF1A & MDM2) ( probability: 0.0625, error: 1)
## MDM2 = (HIF1A & MDM2) | (EP300 & !HIF1A & !MDM2) ( probability: 0.0625, error: 1)
## MDM2 = (!EP300 & !HIF1A & MDM2) | (EP300 & !HIF1A & !MDM2) | (EP300 & HIF1A & MDM2) ( probability: 0
## MDM2 = (!EP300 & MDM2) | (EP300 & !HIF1A & !MDM2) | (HIF1A & MDM2) ( probability: 0.0625, error: 1)
##
## Alternative transition functions for gene TP53:
## TP53 = (!EP300 & !MDM2) | (EP300 & MDM2) ( probability: 0.5, error: 1)
## TP53 = (!EP300) | (MDM2) ( probability: 0.5, error: 1)
##
## Alternative transition functions for gene VHL:
## VHL = (!MDM2 & !VHL) | (!HIF1A & MDM2 & VHL) | (HIF1A & !MDM2) | (HIF1A & !VHL) ( probability: 0.25,
## VHL = (!MDM2 & !VHL) | (MDM2 & VHL) | (HIF1A) ( probability: 0.25, error: 1)
## VHL = (!VHL) | (!HIF1A & MDM2) | (HIF1A & !MDM2) ( probability: 0.25, error: 1)
## VHL = (!VHL) | (MDM2) | (HIF1A) ( probability: 0.25, error: 1)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## O2 = 0
```

```
# Individual nets of each replica:

net <- reconstructNetwork(glioma1x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```

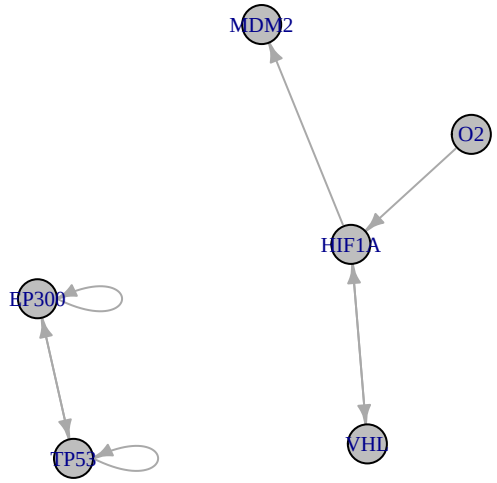



```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (!VHL) ( probability: 1, error: 0)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = 0 ( probability: 1, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = 0 ( probability: 1, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = (!O2) ( probability: 0.25, error: 0)
## TP53 = (!MDM2) ( probability: 0.25, error: 0)
## TP53 = (!HIF1A) ( probability: 0.25, error: 0)
## TP53 = (!EP300) ( probability: 0.25, error: 0)
##
## Alternative transition functions for gene VHL:
```

```
## VHL = (TP53) ( probability: 1, error: 0)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## HIF1A = 0
## MDM2 = 0
## O2 = 0
```

```
net <- reconstructNetwork(glioma2x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```

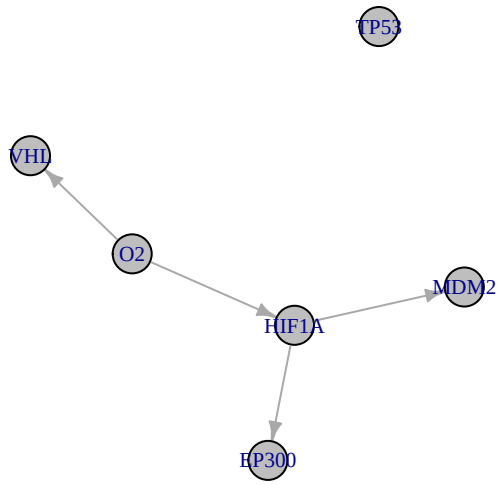



```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (!TP53) ( probability: 0.5, error: 0)
## EP300 = (!EP300) ( probability: 0.5, error: 0)
```

```
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (O2) ( probability: 0.5, error: 0)
## HIF1A = (!VHL) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (!HIF1A) ( probability: 1, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = (!TP53) ( probability: 0.5, error: 0)
## TP53 = (!EP300) ( probability: 0.5, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (HIF1A) ( probability: 1, error: 0)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## O2 = 0
```

```
net <- reconstructNetwork(glioma3x, method="bestfit",returnPBN=TRUE,readableFunctions=TRUE)
plotNetworkWiring(net)
```



```
print(net)
```

```
## Probabilistic Boolean network with 6 genes
##
## Involved genes:
## EP300 HIF1A MDM2 TP53 VHL O2
##
## Transition functions:
##
## Alternative transition functions for gene EP300:
## EP300 = (HIF1A) ( probability: 1, error: 0)
##
## Alternative transition functions for gene HIF1A:
## HIF1A = (O2) ( probability: 1, error: 0)
##
## Alternative transition functions for gene MDM2:
## MDM2 = (HIF1A) ( probability: 1, error: 0)
##
## Alternative transition functions for gene TP53:
## TP53 = 1 ( probability: 1, error: 0)
##
## Alternative transition functions for gene VHL:
## VHL = (!O2) ( probability: 1, error: 0)
##
## Alternative transition functions for gene O2:
## O2 = 0 ( probability: 1, error: 0)
##
## Knocked-out and over-expressed genes:
## TP53 = 1
## O2 = 0
```