

BoolNet

```
library(BoolNet)
setwd("/data4/terrematte/modelling/BoolNet")
```

Boolean network from HIFaxis 10/09/2020

```
net <- loadNetwork("boolean_network_HIFaxis.bn")
```

```
## Warning in readLines(file, -1): linha final incompleta encontrada em
## 'boolean_network_HIFaxis.bn'
```

```
## Warning in loadNetwork("boolean_network_HIFaxis.bn"): There is no transition
## function for gene "GFs"! Assuming an input!
```

```
net
```

```
## Boolean network with 16 genes
##
## Involved genes:
## O2 VHL HIF1a HIF2a p53 REDD1 mTOR AKT mdm2 PLC p300 cMyc VEGF BNIP3 TCF3 GFs
##
## Transition functions:
## O2 = 0
## VHL = O2 & !PLC
## HIF1a = !VHL & ((!p53 & p300) & !mdm2)
## HIF2a = !HIF1a & !VHL & (p300 | mTOR)
## p53 = ((! O2 & ((!HIF1a & p300) & !mdm2)) | HIF1a) | (!VHL & !HIF2a)
## REDD1 = HIF1a
## mTOR = GFs & !REDD1 & !BNIP3 | (HIF2a & !VHL)
## AKT = mTOR
## mdm2 = AKT & p53
## PLC = GFs
## p300 = PLC
## cMyc = HIF2a & !HIF1a
## VEGF = HIF1a | HIF2a
## BNIP3 = HIF1a
## TCF3 = HIF1a
## GFs = GFs
##
## Knocked-out and over-expressed genes:
## O2 = 0
```

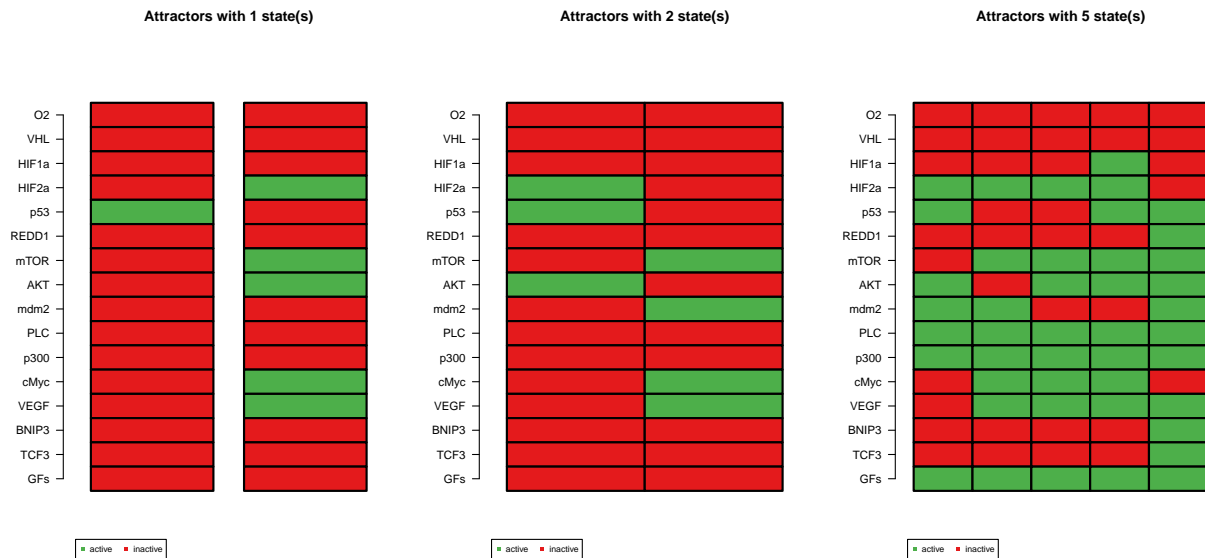
```

attr.syn <- getAttractors(net, type = "synchronous")

# calculate number of different attractor lengths,
# and plot attractors side by side in "table" mode
par(mfrow=c(1, length(table(sapply(attr.syn$attractors,
                                   function(attr.syn)
                                   {
                                     length(attr.syn$involvedStates)
                                   }))))))

plotAttractors(attr.syn)

```



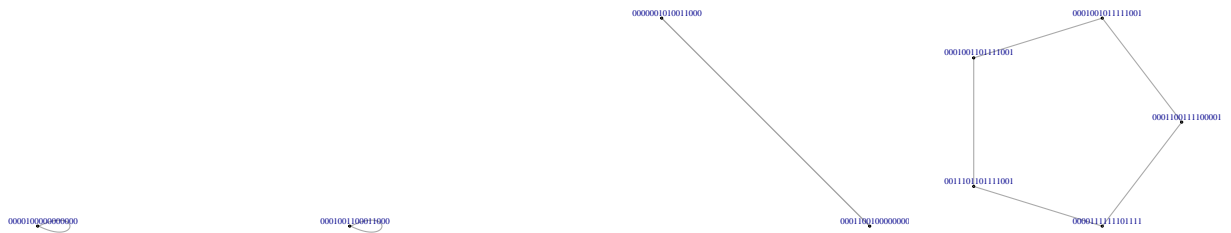
```

## $`1`
##      Attr1.1 Attr2.1
## O2          0      0
## VHL          0      0
## HIF1a        0      0
## HIF2a        0      1
## p53          1      0
## REDD1        0      0
## mTOR         0      1
## AKT          0      1
## mdm2         0      0
## PLC          0      0
## p300         0      0
## cMyc         0      1
## VEGF         0      1
## BNIP3        0      0
## TCF3         0      0
## GFs         0      0
##
## $`2`

```

```
##      Attr3.1 Attr3.2
## O2      0      0
## VHL      0      0
## HIF1a    0      0
## HIF2a    1      0
## p53      1      0
## REDD1    0      0
## mTOR      0      1
## AKT      1      0
## mdm2      0      1
## PLC      0      0
## p300      0      0
## cMyc      0      1
## VEGF      0      1
## BNIP3    0      0
## TCF3      0      0
## GFs      0      0
##
## $`5`
##      Attr4.1 Attr4.2 Attr4.3 Attr4.4 Attr4.5
## O2      0      0      0      0      0
## VHL      0      0      0      0      0
## HIF1a    0      0      0      1      0
## HIF2a    1      1      1      1      0
## p53      1      0      0      1      1
## REDD1    0      0      0      0      1
## mTOR      0      1      1      1      1
## AKT      1      0      1      1      1
## mdm2      1      1      0      0      1
## PLC      1      1      1      1      1
## p300      1      1      1      1      1
## cMyc      0      1      1      1      0
## VEGF      0      1      1      1      1
## BNIP3    0      0      0      0      1
## TCF3      0      0      0      0      1
## GFs      1      1      1      1      1
```

```
# plot attractors in "graph" mode
par(mfrow=c(1, length(attr.syn$attractors)))
plotAttractors(attr.syn, mode="graph")
```

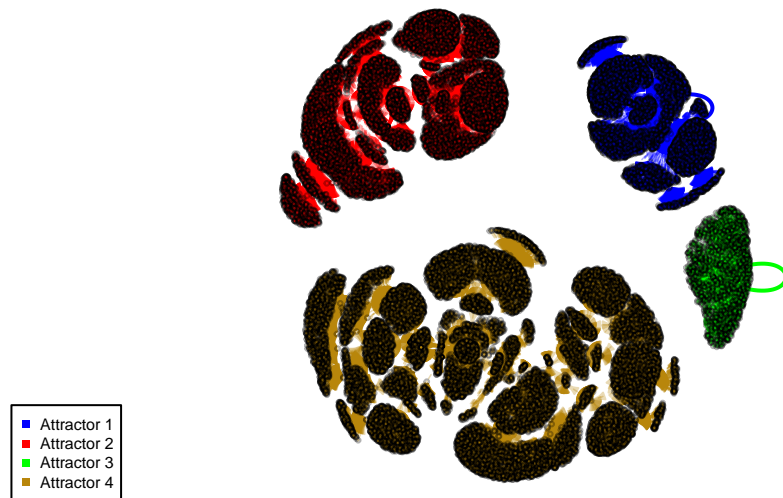


```
# identify asynchronous attractors
attr.asyn <- getAttractors(net, type="asynchronous")

# plot attractors in "graph" mode
par(mfrow=c(1, length(attr.asyn$Attractors)))
plotAttractors(attr.asyn, mode="graph")
```



```
plotStateGraph(attr.syn)
```



```
sim <- markovSimulation(net,
  numIterations=1024,
  returnTable=FALSE)
sim
```

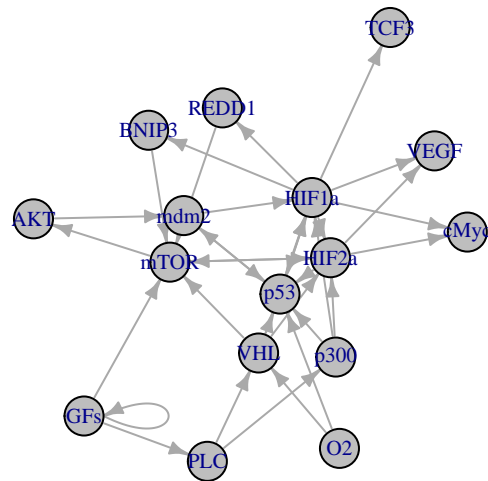
States reached at the end of the simulation:

##	O2	VHL	HIF1a	HIF2a	p53	REDD1	mTOR	AKT	mdm2	PLC	p300	cMyc	VEGF	BNIP3	TCF3	GFs
## 1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
## 2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0
## 3	0	0	0	1	0	0	1	1	0	0	0	1	1	0	0	0
## 4	0	0	0	0	0	0	1	0	1	0	0	1	1	0	0	0
## 5	0	0	0	1	1	0	0	1	1	1	1	0	0	0	0	1
## 6	0	0	0	1	0	0	1	1	0	1	1	1	1	0	0	1
## 7	0	0	1	1	1	0	1	1	0	1	1	1	1	0	0	1
## 8	0	0	0	1	0	0	1	0	1	1	1	1	1	0	0	1
## 9	0	0	0	0	1	1	1	1	1	1	1	0	1	1	1	1

Probability

## 1	0.17578125
## 2	0.24218750
## 3	0.04687500
## 4	0.03515625
## 5	0.13916016
## 6	0.11669922
## 7	0.06298828
## 8	0.04980469
## 9	0.13134766

```
plotNetworkWiring(net)
```



Boolean network from 09/07/2020

```
net <- loadNetwork("boolean_network_2020_07_09.bn")
net
```

```
## Boolean network with 25 genes
```

```
##
```

```
## Involved genes:
```

```
## 02 HIF1a HIF2a p53 BNIP3 VEGF cMyc Oct4 cycD Rb E2F cycE cycA p27 cdc20 cdh1 cycB mdm2 BAD BclX Mito
```

```
##
```

```
## Transition functions:
```

```
## 02 = 0
```

```
## HIF1a = !02 & !mdm2
```

```
## HIF2a = !02 & !HIF1a
```

```
## p53 = !02
```

```
## BNIP3 = HIF1a
```

```
## VEGF = HIF1a | HIF2a
```

```
## cMyc = HIF2a & !HIF1a
```

```
## Oct4 = HIF2a & !HIF1a
```

```
## cycD = 02
```

```

## Rb = (!cycD & !cycE & !cycA & !cycB) | (p27 & !cycD & !cycB)
## E2F = (!Rb & !cycA & !cycB) | (p27 & !Rb & !cycB)
## cycE = E2F & ! Rb
## cycA = (E2F & !Rb & !cdc20) | (cycA & !Rb & !cdc20)
## p27 = ((!cycD & !cycE & !cycA & !cycB) | (p27 & !(cycE & cycA) & !cycB & cycD)) & !cMyc
## cdc20 = cycB & !p53
## cdh1 = (!cycA & !cycB) | cdc20 | (p27 & !cycB)
## cycB = !cdc20 & !cdh1
## mdm2 = p53 & !HIF1a
## BAD = p53 & !Oct4
## BclX = (!BNIP3 | !BAD) & VEGF
## Mito = !BclX & p53
## IAP = VEGF & !Mito
## Apaf = p53
## APC = Mito & Apaf
## casp3 = APC & !IAP
##
## Knocked-out and over-expressed genes:
## O2 = 0

```

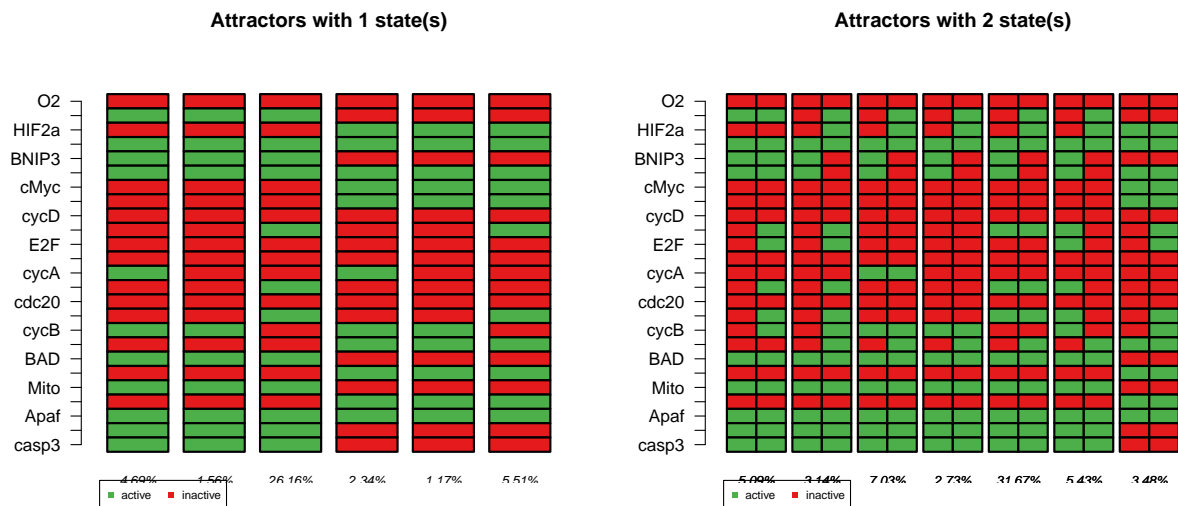
```

attr.syn <- getAttractors(net, type = "synchronous")

# calculate number of different attractor lengths,
# and plot attractors side by side in "table" mode
par(mfrow=c(1, length(table(sapply(attr.syn$attractors,
                                   function(attr.syn)
                                   {
                                     length(attr.syn$involvedStates)
                                   }))))))

plotAttractors(attr.syn)

```



```
## $~1`
```

##	Attr1.1	Attr2.1	Attr3.1	Attr4.1	Attr5.1	Attr6.1		
## 02	0	0	0	0	0	0		
## HIF1a	1	1	1	0	0	0		
## HIF2a	0	0	0	1	1	1		
## p53	1	1	1	1	1	1		
## BNIP3	1	1	1	0	0	0		
## VEGF	1	1	1	1	1	1		
## cMyc	0	0	0	1	1	1		
## Oct4	0	0	0	1	1	1		
## cycD	0	0	0	0	0	0		
## Rb	0	0	1	0	0	1		
## E2F	0	0	0	0	0	0		
## cycE	0	0	0	0	0	0		
## cycA	1	0	0	1	0	0		
## p27	0	0	1	0	0	0		
## cdc20	0	0	0	0	0	0		
## cdh1	0	0	1	0	0	1		
## cycB	1	1	0	1	1	0		
## mdm2	0	0	0	1	1	1		
## BAD	1	1	1	0	0	0		
## BclX	0	0	0	1	1	1		
## Mito	1	1	1	0	0	0		
## IAP	0	0	0	1	1	1		
## Apaf	1	1	1	1	1	1		
## APC	1	1	1	0	0	0		
## casp3	1	1	1	0	0	0		
##								
## \$`2`								
##	Attr7.1	Attr7.2	Attr8.1	Attr8.2	Attr9.1	Attr9.2	Attr10.1	Attr10.2
## 02	0	0	0	0	0	0	0	0
## HIF1a	1	1	0	1	0	1	0	1
## HIF2a	0	0	0	1	0	1	0	1
## p53	1	1	1	1	1	1	1	1
## BNIP3	1	1	1	0	1	0	1	0
## VEGF	1	1	1	0	1	0	1	0
## cMyc	0	0	0	0	0	0	0	0
## Oct4	0	0	0	0	0	0	0	0
## cycD	0	0	0	0	0	0	0	0
## Rb	0	1	0	1	0	0	0	0
## E2F	0	1	0	1	0	0	0	0
## cycE	0	0	0	0	0	0	0	0
## cycA	0	0	0	0	1	1	0	0
## p27	0	1	0	1	0	0	0	0
## cdc20	0	0	0	0	0	0	0	0
## cdh1	0	1	0	1	0	0	0	0
## cycB	0	1	0	1	1	1	1	1
## mdm2	0	0	0	1	0	1	0	1
## BAD	1	1	1	1	1	1	1	1
## BclX	0	0	0	0	0	0	0	0
## Mito	1	1	1	1	1	1	1	1
## IAP	0	0	0	0	0	0	0	0
## Apaf	1	1	1	1	1	1	1	1
## APC	1	1	1	1	1	1	1	1
## casp3	1	1	1	1	1	1	1	1


```
# plot attractors in "graph" mode
par(mfrow=c(1, length(attr.syn$attractors)))
plotAttractors(attr.syn, mode="graph")
```

9

```

# # identify asynchronous attractors
# attr.asyn <- getAttractors(net, type="asynchronous")
#
# # plot attractors in "graph" mode
# par(mfrow=c(1, length(attr.asyn$attractors)))
# plotAttractors(attr.asyn, mode="graph")

```

```

sim <- markovSimulation(net,
                        numIterations=1024,
                        returnTable=FALSE)
sim

```

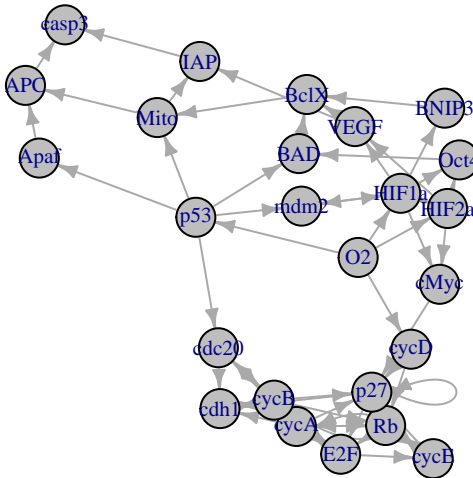
States reached at the end of the simulation:

##	02	HIF1a	HIF2a	p53	BNIP3	VEGF	cMyc	Oct4	cycD	Rb	E2F	cycE	cycA	p27	cdc20	cdh1
## 1	0	0	1	1	0	1	1	1	0	0	0	0	0	0	0	0
## 2	0	0	1	1	0	1	1	1	0	1	0	0	0	0	0	1
## 3	0	0	1	1	0	1	1	1	0	0	0	0	0	0	0	0
## 4	0	0	1	1	0	1	1	1	0	0	0	0	1	0	0	0
## 5	0	0	1	1	0	1	1	1	0	1	1	0	0	0	0	1
## 6	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0
## 7	0	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0
## 8	0	0	0	1	1	1	0	0	0	1	0	0	0	1	0	1
## 9	0	1	0	1	1	1	0	0	0	1	0	0	0	1	0	1
## 10	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0
## 11	0	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0
## 12	0	0	0	1	1	1	0	0	0	0	0	0	1	0	0	0
## 13	0	1	0	1	1	1	0	0	0	0	0	0	1	0	0	0
## 14	0	0	0	1	1	1	0	0	0	1	1	0	0	1	0	1
## 15	0	1	0	1	1	1	0	0	0	1	1	0	0	1	0	1
## 16	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
## 17	0	1	1	1	0	0	0	0	0	1	0	0	0	1	0	1
## 18	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
## 19	0	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0
## 20	0	1	1	1	0	0	0	0	0	1	1	0	0	1	0	1

##	cycB	mdm2	BAD	BclX	Mito	IAP	Apaf	APC	casp3	Probability
## 1	0	1	0	1	0	1	1	0	0	0.019531250
## 2	0	1	0	1	0	1	1	0	0	0.055053711
## 3	1	1	0	1	0	1	1	0	0	0.011718750
## 4	1	1	0	1	0	1	1	0	0	0.023437500
## 5	1	1	0	1	0	1	1	0	0	0.015258789
## 6	0	0	1	0	1	0	1	1	1	0.009765625
## 7	0	0	1	0	1	0	1	1	1	0.029296875
## 8	0	0	1	0	1	0	1	1	1	0.064819336
## 9	0	0	1	0	1	0	1	1	1	0.261596680
## 10	1	0	1	0	1	0	1	1	1	0.011718750
## 11	1	0	1	0	1	0	1	1	1	0.015625000
## 12	1	0	1	0	1	0	1	1	1	0.023437500
## 13	1	0	1	0	1	0	1	1	1	0.046875000
## 14	1	0	1	0	1	0	1	1	1	0.015258789
## 15	1	0	1	0	1	0	1	1	1	0.021606445
## 16	0	1	1	0	1	0	1	1	1	0.039062500
## 17	0	1	1	0	1	0	1	1	1	0.251831055
## 18	1	1	1	0	1	0	1	1	1	0.015625000

```
## 19      1      1      1      0      1      0      1      1      1 0.046875000
## 20      1      1      1      0      1      0      1      1      1 0.021606445
```

```
plotNetworkWiring(net)
```



Boolean network from 10/06/2020

```
net <- loadNetwork("boolean_network_2020_06_10.bn")
```

```
## Warning in loadNetwork("boolean_network_2020_06_10.bn"): There is no transition
## function for gene "Space"! Assuming an input!
```

```
## Warning in loadNetwork("boolean_network_2020_06_10.bn"): There is no transition
## function for gene "Mito"! Assuming an input!
```

```
net
```

```
## Boolean network with 26 genes
```

```
##
```

```
## Involved genes:
```

```
## 02 HIF1a HIF2a cMyc cycD Rb E2F cycE cycA p27 cdc20 cdh1 cycB akt mdm2 p53 NFkB BNIP3 BAD BclX IAP Apo
```

```

##
## Transition functions:
## O2 = 0
## HIF1a = !O2
## HIF2a = !HIF1a
## cMyc = HIF2a
## cycD = !HIF1a
## Rb = (!cycD & !cycE & !cycA & !cycB) | (p27 & !cycD & !cycB)
## E2F = (!Rb & !cycA & !cycB) | (p27 & !Rb & !cycB)
## cycE = E2F & !Rb
## cycA = (E2F & !Rb & !cdc20) | (cycA & !Rb & !cdc20)
## p27 = (!cycD & !cycE & !cycA & !cycB) | (cMyc & !(cycE & cycA) & !cycB & cycD)
## cdc20 = cycB & !p53
## cdh1 = (!cycA & !cycB) | cdc20 | (p27 & !cycB)
## cycB = !cdc20 & !cdh1
## akt = HIF2a
## mdm2 = akt
## p53 = (HIF1a | (O2 & Space)) & !mdm2
## NFkB = O2 & Space
## BNIP3 = HIF1a
## BAD = p53
## BclX = (!BNIP3 | !BAD) & NFkB
## IAP = NFkB & !Mito
## Apaf = p53
## APC = Mito & Apaf
## casp3 = APC & !IAP
## Space = Space
## Mito = Mito
##
## Knocked-out and over-expressed genes:
## O2 = 0

```

```

attr.syn <- getAttractors(net, type = "synchronous")

# calculate number of different attractor lengths,
# and plot attractors side by side in "table" mode
par(mfrow=c(1, length(table(sapply(attr.syn$attractors,
                                   function(attr.syn)
                                   {
                                     length(attr.syn$involvedStates)
                                   }))))))

plotAttractors(attr.syn)

```



```
## $`1`
##      Attr1.1 Attr2.1 Attr3.1 Attr4.1 Attr5.1 Attr6.1 Attr7.1 Attr8.1 Attr9.1
## O2      0      0      0      0      0      0      0      0      0
## HIF1a    1      1      1      1      1      1      1      1      1
## HIF2a    0      0      0      0      0      0      0      0      0
## cMyc     0      0      0      0      0      0      0      0      0
## cycD     0      0      0      0      0      0      0      0      0
## Rb       1      0      0      1      0      0      1      0      0
## E2F      0      0      0      0      0      0      0      0      0
## cycE     0      0      0      0      0      0      0      0      0
## cycA     0      1      0      0      1      0      0      1      0
## p27      1      0      0      1      0      0      1      0      0
## cdc20    0      0      0      0      0      0      0      0      0
## cdh1     1      0      0      1      0      0      1      0      0
## cycB     0      1      1      0      1      1      0      1      1
## akt      0      0      0      0      0      0      0      0      0
## mdm2     0      0      0      0      0      0      0      0      0
## p53      1      1      1      1      1      1      1      1      1
## NFkB     0      0      0      0      0      0      0      0      0
## BNIP3    1      1      1      1      1      1      1      1      1
## BAD      1      1      1      1      1      1      1      1      1
## BclX     0      0      0      0      0      0      0      0      0
## IAP      0      0      0      0      0      0      0      0      0
## Apaf     1      1      1      1      1      1      1      1      1
## APC      0      0      0      0      0      0      1      1      1
## casp3    0      0      0      0      0      0      1      1      1
## Space    0      0      0      1      1      1      0      0      0
## Mito     0      0      0      0      0      0      1      1      1
##      Attr10.1 Attr11.1 Attr12.1
## O2      0      0      0
## HIF1a    1      1      1
## HIF2a    0      0      0
## cMyc     0      0      0
```

```

## cycD      0      0      0
## Rb        1      0      0
## E2F       0      0      0
## cycE      0      0      0
## cycA      0      1      0
## p27       1      0      0
## cdc20     0      0      0
## cdh1      1      0      0
## cycB      0      1      1
## akt       0      0      0
## mdm2      0      0      0
## p53       1      1      1
## NFkB      0      0      0
## BNIP3     1      1      1
## BAD       1      1      1
## BclX      0      0      0
## IAP       0      0      0
## Apaf      1      1      1
## APC       1      1      1
## casp3     1      1      1
## Space     1      1      1
## Mito      1      1      1
##
## $`2`
##      Attr13.1 Attr13.2 Attr14.1 Attr14.2 Attr15.1 Attr15.2 Attr16.1 Attr16.2
## O2      0      0      0      0      0      0      0      0
## HIF1a    1      1      1      1      1      1      1      1
## HIF2a    0      0      0      0      0      0      0      0
## cMyc     0      0      0      0      0      0      0      0
## cycD     0      0      0      0      0      0      0      0
## Rb       0      1      0      1      0      1      0      1
## E2F      0      1      0      1      0      1      0      1
## cycE     0      0      0      0      0      0      0      0
## cycA     0      0      0      0      0      0      0      0
## p27      0      1      0      1      0      1      0      1
## cdc20    0      0      0      0      0      0      0      0
## cdh1     0      1      0      1      0      1      0      1
## cycB     0      1      0      1      0      1      0      1
## akt      0      0      0      0      0      0      0      0
## mdm2     0      0      0      0      0      0      0      0
## p53      1      1      1      1      1      1      1      1
## NFkB     0      0      0      0      0      0      0      0
## BNIP3    1      1      1      1      1      1      1      1
## BAD      1      1      1      1      1      1      1      1
## BclX     0      0      0      0      0      0      0      0
## IAP      0      0      0      0      0      0      0      0
## Apaf     1      1      1      1      1      1      1      1
## APC      0      0      0      0      1      1      1      1
## casp3    0      0      0      0      1      1      1      1
## Space    0      0      1      1      0      0      1      1
## Mito     0      0      0      0      1      1      1      1

```

```

# # plot attractors in "graph" mode
# par(mfrow=c(1, length(attr.syn$attractors)))

```

```
# plotAttractors(attr.syn, mode="graph")

# # identify asynchronous attractors
# attr.asyn <- getAttractors(net, type="asynchronous")
#
# # plot attractors in "graph" mode
# par(mfrow=c(1, length(attr.asyn$attractors)))
# plotAttractors(attr.asyn, mode="graph")
```

```
plotNetworkWiring(net)
```

