

Supplementary Material for Directional tests in Gaussian graphical models

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1 Introduction

The current report reproduces the Figures and numerical results in Sections 5 and 6 of the main text. The outputs have been produced using R version 4.2.2 (R Core Team 2020). The code chunk below loads the necessary R packages.

```
library(matrixcalc)
library(Matrix)
library(mvtnorm)
library(ggm)
library(Rgraphviz)
library(gRbase)
library(igraph)
```

We also provide code to reproduce all simulation results in the paper. The R scripts to carry out the simulation experiments, and the results from those, are provided in the `DirInfGGM_code+results.zip` archive. `res_dir` is the directory where the contents of the archive are and needs to be set appropriately.

```
res_dir <- "~/Dropbox/Directional/Supplementary/DirInfGGM_code+results"
```

2 Simulation studies

This section provides the R code that reproduces the outputs of Section 5 in the paper.

2.1 Scenario 1

The code chunk below opens in Macbook laptops an XQuartz window giving the chordal graph considered under the alternative hypothesis. Figure 1 was obtained by modifying this accordingly, and then exporting the resulting alternative (left) and null (right) graphs to two different PDF files that were juxtaposed in the main text.

```
ug1 <- UG(~ A*B + B*C + B*D + B*E + C*E + D*E + E*F)
graph1 <- graph.adjacency(ug1, mode = "undirected", diag = FALSE)

x <- tkplot(graph1, vertex.color = "lightgrey", vertex.label.color = "black",
            vertex.label.family = "Arial", vertex.size = 15, vertex.label.cex = 1.5)
```

The following code chunk uses the image `dir_small_res.rda` to reproduce Figure 6 of the main text. `dir_small_res.rda` results by running the script `simulations1.R`, available in the supplementary code archive.

```

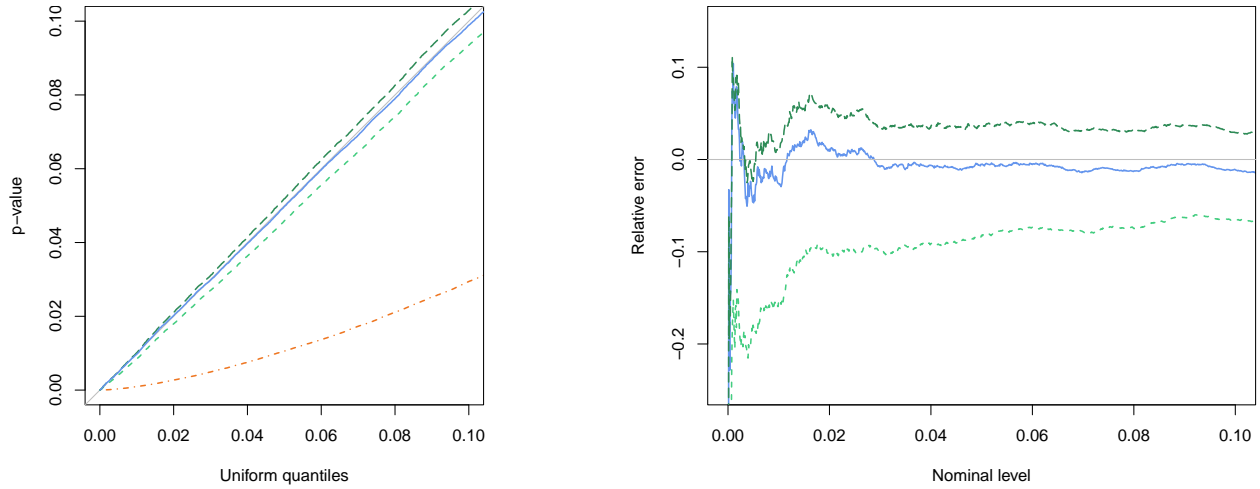
setwd(res_dir)
load("dir_small_res.rda")

par(mfrow = c(1, 2), mai = c(1, 1, 0, 0.5))
old.pty <- par("pty")
par(pty = "s")
# 1st plot: empirical p-values
index <- seq(1, length(res_small$first.order), by = 10)
x <- sort(res_small$first.order)
x <- x[index]
plot(ppoints(x), x, type = "l",
     xlim= c(0, 0.1), lwd = 1.5, ylim= c(0, 0.1), xlab = "Uniform quantiles",
     ylab = "p-value", pty = "s", col = "chocolate2", lty = "dotdash", cex.lab = 1)
abline(0, 1, col = "grey")
x <- sort(res_small$skovgaard1)
x <- x[index]
lines(ppoints(x), x, col = "seagreen3",
      lwd = 1.5, lty = "dashed")
x <- sort(res_small$skovgaard2)
x <- x[index]
lines(ppoints(x), x, col = "seagreen4",
      lty = "longdash", lwd = 1.5)
x <- sort(res_small$directional)
x <- x[index]
lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)

par(pty = old.pty)

# 2nd plot: relative error for p-values lower than 0.10 (without first-order)
x <- sort(res_small$directional)
x <- x[index]
plot(ppoints(x), (x - ppoints(x))/ppoints(x), xlim = c(0, 0.1), lwd = 1.5,
     ylab = "Relative error", xlab = "Nominal level", type = "l", ylim = c(-0.25, 0.15),
     cex.lab = 1, col = "cornflowerblue")
abline(h = 0, col = "grey")
x <- sort(res_small$skovgaard1)
x <- x[index]
lines(ppoints(x), (x - ppoints(x))/ppoints(x),
      col = "seagreen3", lty = "dashed", lwd = 1.5)
x <- sort(res_small$skovgaard2)
x <- x[index]
lines(ppoints(x), (x - ppoints(x))/ppoints(x), lwd = 1.5,
      col = "seagreen4", lty = "longdash")

```



2.2 Scenario 2

The code chunk below uses the image `dir_MDq11_res.rda` to reproduce Table 1 of the main text. Tables 2 and 3 are obtained similarly starting from the files `dir_MDq30_res.rda` and `dir_MDq50_res.rda`, respectively. All these images result by running the script `simulations2.R`, available in the supplementary code archive.

```
summary.sim <- function(out, levels = c(0.01, 0.025, 0.05, 0.10, 0.25, 0.5, 0.75,
                                         0.9, 0.95, 0.975, 0.99)) {
  fo <- sapply(levels, function(x) mean(out$first.order < x))
  sk1 <- sapply(levels, function(x) mean(out$skovgaard1 < x))
  sk2 <- sapply(levels, function(x) mean(out$skovgaard2 < x))
  dir2 <- sapply(levels, function(x) mean(out$directional < x))

  sim.se <- sqrt(levels * (1 - levels)/length(out$first.order))
  res <- rbind(levels, fo, sk1, sk2, dir2, sim.se)
  rownames(res) <- c("nominal", "first-order", "Skovgaard W*",
                    "Skovgaard W**", "directional", "sim-error")
  res
}

setwd(res_dir)
load("dir_MDq11_res.rda")

res9md <- round(summary.sim(resMD9), 3)
res6md <- round(summary.sim(resMD6), 3)
res3md <- round(summary.sim(resMD3), 3)
res2md <- round(summary.sim(resMD2), 3)

tab1 <- rbind(res2md[2:5,], res3md[2:5,],
              res6md[2:5,], res9md[2:5,])
round(tab1 * 100, digits = 1)
```

##	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]	[,7]	[,8]	[,9]	[,10]	[,11]
## first-order	1.4	3.3	6.3	12.0	28.4	53.7	77.5	91.2	95.6	97.8	99.1
## Skovgaard W*	1.0	2.5	5.1	10.0	25.1	50.2	75.1	89.9	94.9	97.4	99.0
## Skovgaard W**	1.0	2.5	5.1	10.0	25.1	50.2	75.1	89.9	94.9	97.4	99.0
## directional	1.0	2.5	5.1	10.0	25.2	50.3	75.2	90.1	95.0	97.5	99.0
## first-order	1.8	3.9	7.2	13.5	30.4	56.1	79.3	92.0	96.0	98.1	99.2

## Skovgaard W*	1.1	2.6	5.0	10.0	24.6	49.6	74.6	89.6	94.7	97.3	98.9
## Skovgaard W**	1.0	2.5	5.0	9.9	24.5	49.5	74.5	89.5	94.7	97.2	98.9
## directional	1.0	2.6	5.1	10.1	25.0	50.3	75.4	90.2	95.0	97.5	99.0
## first-order	2.5	5.5	9.8	17.4	36.2	62.2	83.3	94.0	97.2	98.6	99.5
## Skovgaard W*	0.8	2.1	4.3	8.8	22.4	46.4	71.7	87.8	93.6	96.6	98.5
## Skovgaard W**	0.8	2.1	4.2	8.6	22.0	45.9	71.2	87.5	93.4	96.4	98.5
## directional	1.0	2.5	4.9	10.0	25.0	50.3	75.3	90.2	95.1	97.5	99.0
## first-order	3.3	6.9	12.0	20.6	40.8	66.2	85.9	95.2	97.8	99.0	99.6
## Skovgaard W*	0.7	1.8	3.7	7.8	20.7	43.7	69.1	86.3	92.6	96.1	98.2
## Skovgaard W**	0.7	1.8	3.6	7.5	20.1	42.8	68.2	85.7	92.2	95.8	98.1
## directional	1.0	2.4	4.9	9.9	25.2	50.0	75.0	90.1	95.1	97.5	99.0

The following code chunk uses the image `dir_MDq30_res.rda` to reproduce Figure 3 of the main text.

```
plot3.sim <- function(out, out1, out2, out3, step = 10) {
  index <- seq(1, length(out$first.order), by = step)
  par(mfrow = c(2, 2), cex = 0.6, mai = c(0.4, 0.8, 0.15, 0), mex = 0.8,
      pty = "s", oma = c(0.2, 0.2, 0.2, 0.2), mgp = c(3, 1, 0))
  x <- sort(out$first.order)
  x <- x[index]
  plot(ppoints(x), x, xlab = ' ', ylab = '', pch = ".", axes = FALSE, type = "l",
       xlim = c(0, 1), lwd = 1.5, ylim = c(0, 1), col = "chocolate2", lty = "dotdash")
  abline(0, 1, col = "grey")
  x <- sort(out$directional)
  x <- x[index]
  lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)
  x <- sort(out$skovgaard1)
  x <- x[index]
  lines(ppoints(x), x, col = "seagreen3",
       lwd = 1.5, lty = "dashed")
  x <- sort(out$skovgaard2)
  x <- x[index]
  lines(ppoints(x), x, col = "seagreen4",
       lty = "longdash", lwd = 1.5)
  box()
  axis(2)
  axis(1)
  title("vs MD(2)", line = 2, cex.main = 1.5)
  title(ylab = "p-value", cex.lab = 1, line = 3)

  x <- sort(out1$first.order)
  x <- x[index]
  plot(ppoints(x), x, xlab = ' ', ylab = '', pch = ".", axes = FALSE, type = "l",
       xlim = c(0, 1), lwd = 1.5, ylim = c(0, 1), lty = "dotdash", col = "chocolate2")
  abline(0, 1, col = "grey")
  x <- sort(out1$skovgaard1)
  x <- x[index]
  lines(ppoints(x), x, col = "seagreen3",
       lwd = 1.5, lty = "dashed")
  x <- sort(out1$skovgaard2)
  x <- x[index]
  lines(ppoints(x), x, col = "seagreen4",
       lty = "longdash", lwd = 1.5)
  x <- sort(out1$directional)
  x <- x[index]
```

```

lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)
box()
axis(2)
axis(1)
title("vs MD(9)", line = 2, cex.main = 1.5)

x <- sort(out2$first.order)
x <- x[index]
plot(ppoints(x), x, xlab = ' ', ylab = '', pch = ".", axes = FALSE, type = "l",
      xlim = c(0, 1), lwd = 1.5, ylim = c(0, 1), lty = "dotdash", col = "chocolate2")
abline(0, 1, col = "grey")
x <- sort(out2$skovgaard1)
x <- x[index]
lines(ppoints(x), x, col = "seagreen3",
      lwd = 1.5, lty = "dashed")
x <- sort(out2$skovgaard2)
x <- x[index]
lines(ppoints(x), x, col = "seagreen4",
      lty = "longdash", lwd = 1.5)
x <- sort(out2$directional)
x <- x[index]
lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)
box()
axis(2)
axis(1)
title(xlab = "Uniform quantiles", cex.lab = 1, line = 5)
title("vs MD(18)", line = 2, cex.main = 1.5)
title(ylab = "p-value", cex.lab = 1, line = 3)

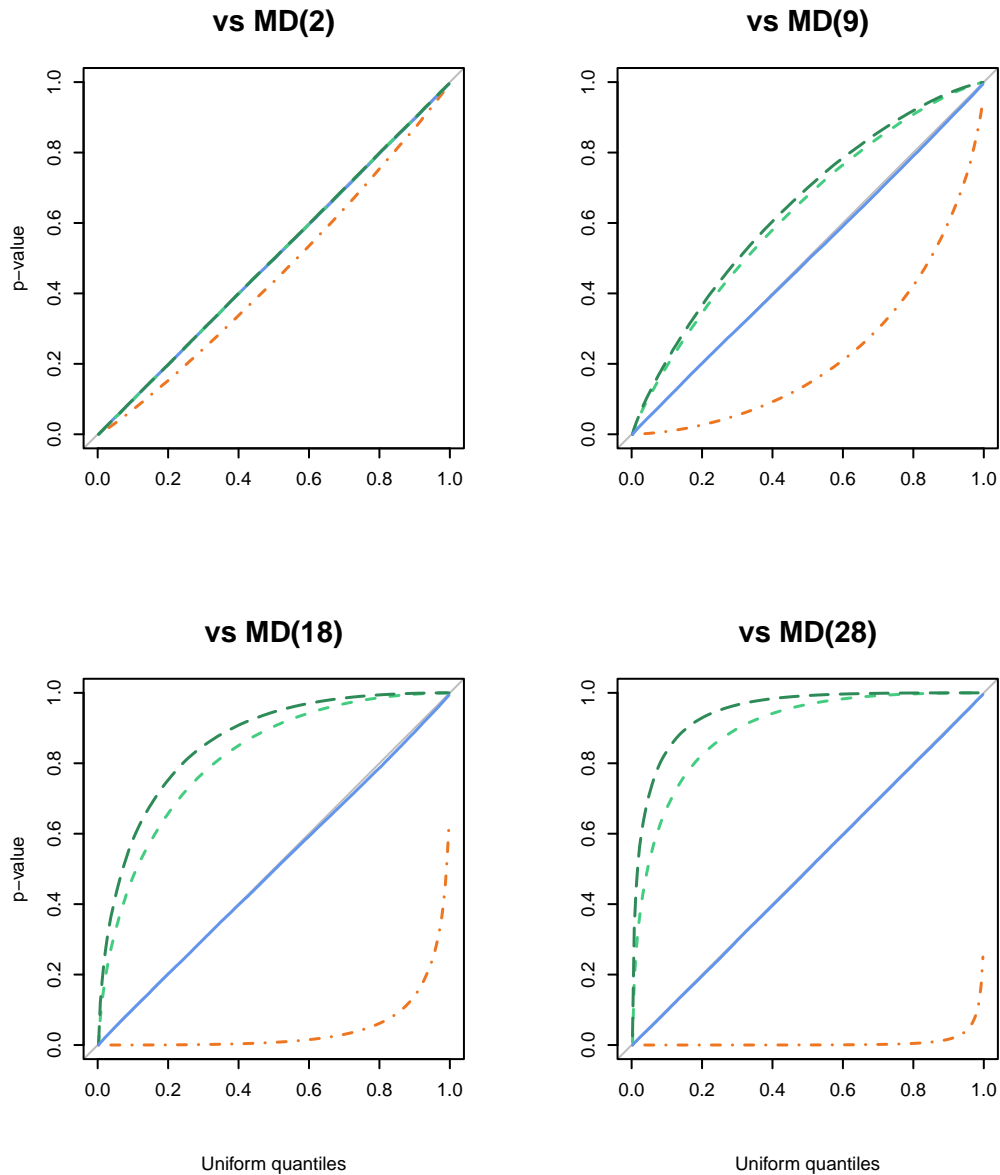
x <- sort(out3$first.order)
x <- x[index]
plot(ppoints(x), x, xlab = ' ', ylab = '', pch = ".", axes = FALSE, type = "l",
      xlim = c(0, 1), lwd = 1.5, ylim = c(0, 1), lty = "dotdash", col = "chocolate2")
abline(0, 1, col = "grey")
x <- sort(out3$skovgaard1)
x <- x[index]
lines(ppoints(x), x, col = "seagreen3",
      lwd = 1.5, lty = "dashed")
x <- sort(out3$skovgaard2)
x <- x[index]
lines(ppoints(x), x, col = "seagreen4",
      lty = "longdash", lwd = 1.5)
x <- sort(out3$directional)
x <- x[index]
lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)
box()
axis(2)
axis(1)
title(xlab = "Uniform quantiles", cex.lab = 1, line = 5)
title("vs MD(28)", line = 2, cex.main = 1.5)
}

setwd(res_dir)

```

```
load("dir_MDq30_res.rda")

plot3.sim(resMD2, resMD9, resMD18, resMD28, step = 500)
```



2.3 Scenario 3

The following two code chunks use the image `dir_block_res.rda` to reproduce Table 4 and Figure 4, respectively, of the main text. The file `dir_block_res.rda` results by running the script `simulations3.R`, available in the supplementary code archive.

```
setwd(res_dir)
load("dir_block_res.rda")

res40n <- round(summary.sim(res40n), 3)
res60n <- round(summary.sim(res60n), 3)
```

```
res90n <- round(summary.sim(res90n), 3)
res120n <- round(summary.sim(res120n), 3)
```

```
tab4 <- rbind(res40n[2:5,], res60n[2:5,],
              res90n[2:5,], res120n[2:5,])
round(tab4 * 100, digits = 1)
```

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]	[,7]	[,8]	[,9]	[,10]	[,11]
## first-order	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
## Skovgaard W*	27.1	39.1	50.6	63.5	81.7	93.7	98.5	99.7	99.9	100.0	100.0
## Skovgaard W**	0.7	1.7	3.4	7.2	19.3	42.0	68.0	85.9	92.5	96.1	98.3
## directional	1.0	2.5	5.0	10.1	25.2	50.2	75.2	90.0	94.9	97.4	98.9
## first-order	98.4	99.3	99.7	99.9	100.0	100.0	100.0	100.0	100.0	100.0	100.0
## Skovgaard W*	2.4	5.3	9.6	17.3	36.6	62.9	84.2	94.6	97.6	98.9	99.6
## Skovgaard W**	0.6	1.7	3.5	7.5	20.4	43.9	70.3	87.4	93.5	96.7	98.6
## directional	1.0	2.5	5.0	10.0	25.1	50.1	75.2	90.2	95.1	97.6	99.0
## first-order	65.9	77.1	85.0	91.5	97.3	99.4	99.9	100.0	100.0	100.0	100.0
## Skovgaard W*	1.3	3.2	6.1	12.0	28.5	54.2	78.2	91.7	96.0	98.1	99.2
## Skovgaard W**	0.8	2.1	4.3	8.9	23.0	47.6	73.2	89.0	94.5	97.2	98.8
## directional	0.9	2.5	5.0	10.1	25.0	50.1	75.1	90.1	95.1	97.6	99.0
## first-order	36.6	50.0	61.6	73.6	88.6	96.7	99.3	99.9	100.0	100.0	100.0
## Skovgaard W*	1.1	2.9	5.6	11.0	26.8	52.2	76.5	90.9	95.5	97.8	99.1
## Skovgaard W**	0.9	2.3	4.6	9.4	24.0	48.7	73.9	89.4	94.6	97.3	98.9
## directional	1.0	2.5	5.0	10.1	25.1	50.1	75.0	90.0	95.0	97.5	99.0

```
plot4.sim <- function(out, out1, out2, out3, step = 10) {
  index <- seq(1, length(out$first.order), by = step)
  par(mfrow = c(2, 2), cex = 0.6, mai = c(0.4, 0.8, 0.15, 0), mex = 0.8,
      pty = "s", oma = c(0.2, 0.2, 0.2, 0.2), mgp = c(3, 1, 0))
  x <- sort(out$first.order)
  x <- x[index]
  plot(ppoints(x), x, xlab = ' ', ylab = '', pch = ".", axes = FALSE, type = "l",
      xlim = c(0, 1), lwd = 1.5, ylim = c(0, 1), col = "chocolate2", lty = "dotted")
  abline(0, 1, col = "grey")
  x <- sort(out$directional)
  x <- x[index]
  lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)
  x <- sort(out$skovgaard1)
  x <- x[index]
  lines(ppoints(x), x, col = "seagreen3",
      lwd = 1.5, lty = "dashed")
  x <- sort(out$skovgaard2)
  x <- x[index]
  lines(ppoints(x), x, col = "seagreen4",
      lty = "longdash", lwd = 1.5)
  box()
  axis(2)
  axis(1)
  title(expression(italic(n) == 40), line = 2, cex.main = 1.5)
  title(ylab = "p-value", cex.lab = 1, line = 3)

  x <- sort(out1$first.order)
  x <- x[index]
  plot(ppoints(x), x, xlab = ' ', ylab = '', pch = ".", axes = FALSE, type = "l",
```

```

        xlim = c(0, 1), lwd = 1.5, ylim = c(0, 1), lty = "dotdash", col = "chocolate2")
abline(0, 1, col = "grey")
x <- sort(out1$skovgaard1)
x <- x[index]
lines(ppoints(x), x, col = "seagreen3",
      lwd = 1.5, lty = "dashed")
x <- sort(out1$skovgaard2)
x <- x[index]
lines(ppoints(x), x, col = "seagreen4",
      lty = "longdash", lwd = 1.5)
x <- sort(out1$directional)
x <- x[index]
lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)
box()
axis(2)
axis(1)
title(expression(italic(n) == 60), line = 2, cex.main = 1.5)

x <- sort(out2$first.order)
x <- x[index]
plot(ppoints(x), x, xlab = ' ', ylab = '', pch = ".", axes = FALSE, type = "l",
     xlim = c(0, 1), lwd = 1.5, ylim = c(0, 1), lty = "dotdash", col = "chocolate2")
abline(0, 1, col = "grey")
x <- sort(out2$skovgaard1)
x <- x[index]
lines(ppoints(x), x, col = "seagreen3",
      lwd = 1.5, lty = "dashed")
x <- sort(out2$skovgaard2)
x <- x[index]
lines(ppoints(x), x, col = "seagreen4",
      lty = "longdash", lwd = 1.5)
x <- sort(out2$directional)
x <- x[index]
lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)
box()
axis(2)
axis(1)
title(xlab = "Uniform quantiles", cex.lab = 1, line = 5)
title(expression(italic(n) == 90), line = 2, cex.main = 1.5)
title(ylab = "p-value", cex.lab = 1, line = 3)

x <- sort(out3$first.order)
x <- x[index]
plot(ppoints(x), x, xlab = ' ', ylab = '', pch = ".", axes = FALSE, type = "l",
     xlim = c(0, 1), lwd = 1.5, ylim = c(0, 1), lty = "dotdash", col = "chocolate2")
abline(0, 1, col = "grey")
x <- sort(out3$skovgaard1)
x <- x[index]
lines(ppoints(x), x, col = "seagreen3",
      lwd = 1.5, lty = "dashed")
x <- sort(out3$skovgaard2)
x <- x[index]
lines(ppoints(x), x, col = "seagreen4",

```



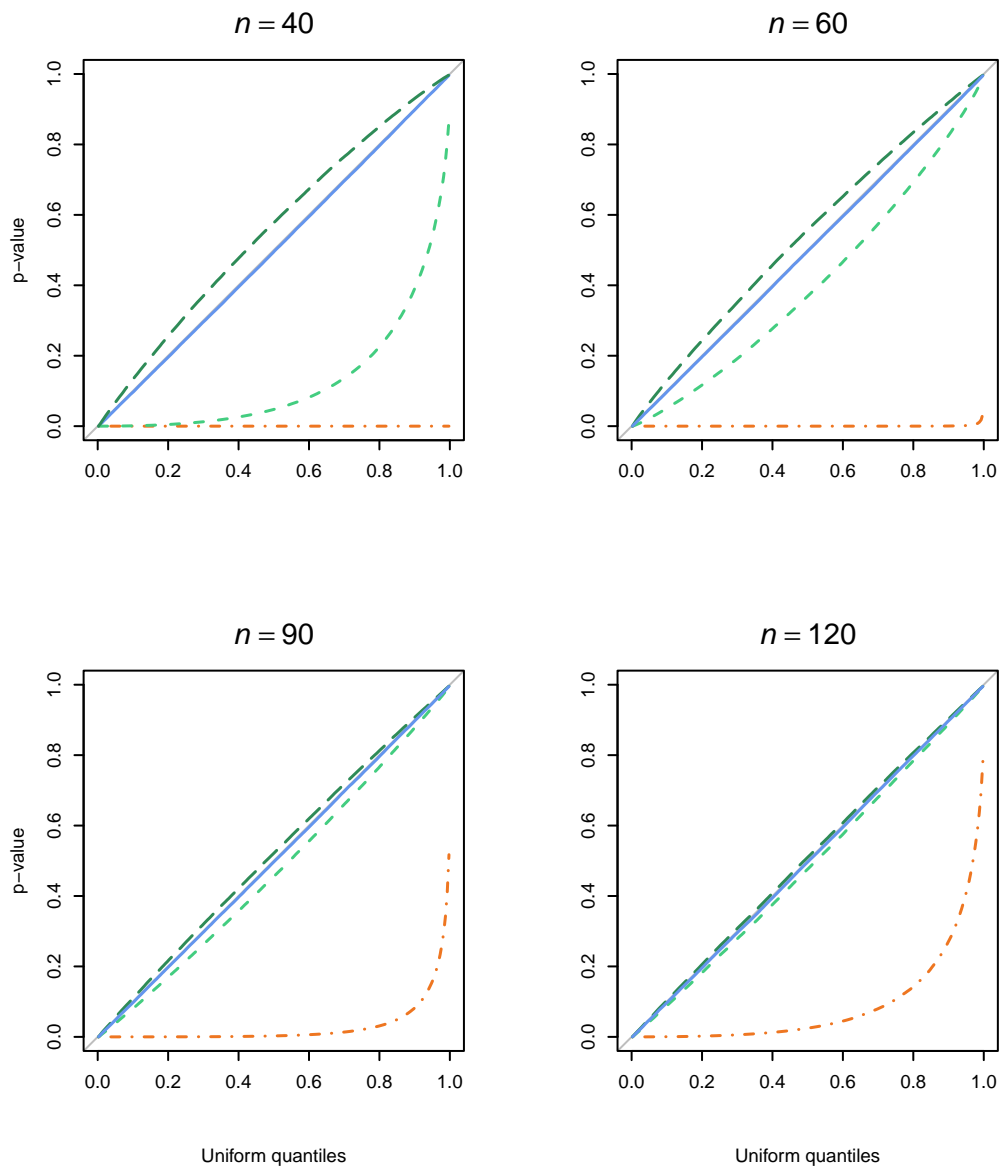
```

    lty = "longdash", lwd = 1.5)
x <- sort(out3$directional)
x <- x[index]
lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)
box()
axis(2)
axis(1)
title(xlab = "Uniform quantiles", cex.lab = 1, line = 5)
title(expression(italic(n) == 120), line = 2, cex.main = 1.5)
}

setwd(res_dir)
load("dir_block_res.rda")

plot4.sim(res40n, res60n, res90n, res120n, step = 500)

```



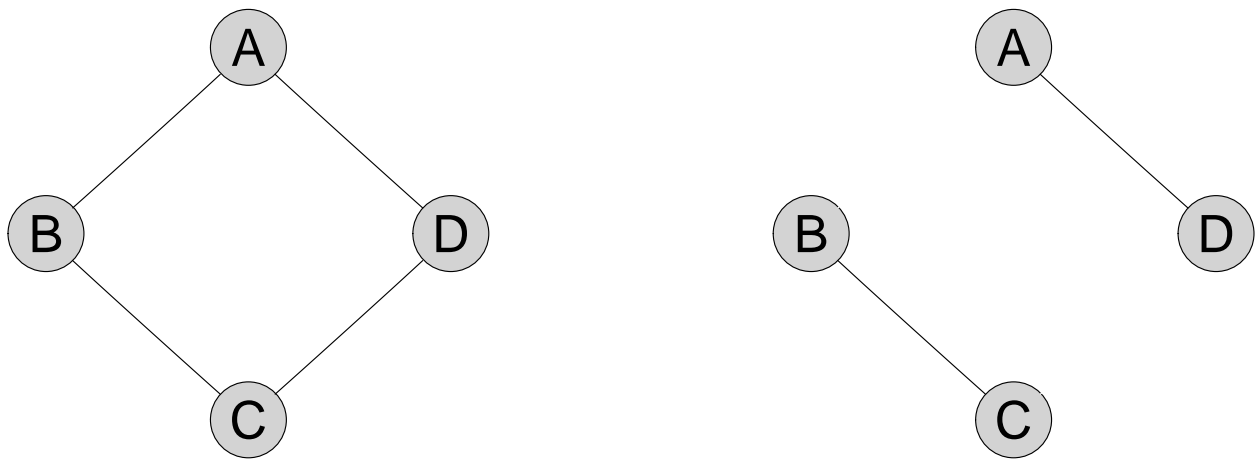
2.4 Scenario 4

The code chunk below reproduces Figure 5.

```
defAttrs <- getDefaultAttrs()
eAttrs <- list()
eAttrs$color <- c("A~B" = "white", "D~C" = "white", "C~B" = "black", "D~A" = "black")

ug0 <- ug(~ A*B + D*C)
ug1 <- ug(~ A*B + D*C + C*B + D*A)

par(mfrow = c(1, 2))
plot(ug1, attrs = list(node = list(fillcolor = "lightgrey", fontsize = "10")))
plot(ug1, edgeAttrs = eAttrs, attrs = list(node = list(fillcolor = "lightgrey",
                                                    fontsize = "10")))
```



The following code chunk uses the image `dir_small_nonch_res.rda` to reproduce Figure 6 of the main text. `dir_small_nonch_res.rda` results by running the script `simulations4.R`, available in the supplementary code archive.

```
setwd(res_dir)
load("dir_small_nonch_res.rda")

par(mfrow = c(1, 2), mai = c(1, 1, 0, 0.5))
old.pty <- par("pty")
par(pty = "s")
# 1st plot: empirical p-values
index <- seq(1, length(res_small_nonch$first.order), by = 10)
x <- sort(res_small_nonch$first.order)
x <- x[index]
plot(ppoints(x), x, type = "l",
     xlim= c(0, 0.1), lwd = 1.5, ylim= c(0, 0.1), xlab = "Uniform quantiles",
     ylab = "p-value", pty = "s", col = "chocolate2", lty = "dotdash", cex.lab = 1)
abline(0, 1, col = "grey")
x <- sort(res_small_nonch$skovgaard1)
x <- x[index]
lines(ppoints(x), x, col = "seagreen3",
      lwd = 1.5, lty = "dashed")
x <- sort(res_small_nonch$skovgaard2)
```

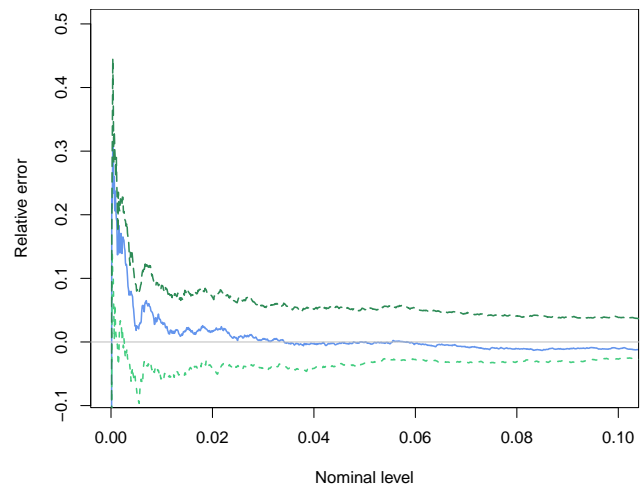
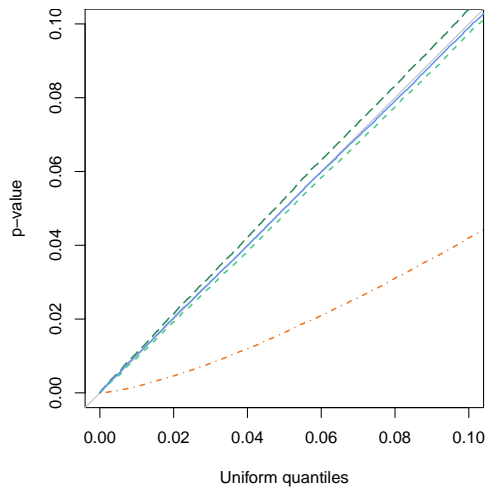
```

x <- x[index]
lines(ppoints(x), x, col = "seagreen4",
      lty = "longdash", lwd = 1.5)
x <- sort(res_small_nonch$directional)
x <- x[index]
lines(ppoints(x), x, col = "cornflowerblue", lwd = 1.5)

par(pty = old.pty)

# 2nd plot: relative error for p-values lower than 0.10 (without w)
x <- sort(res_small_nonch$directional)
x <- x[index]
plot(ppoints(x), (x - ppoints(x))/ppoints(x), xlim = c(0, 0.1), lwd = 1.5,
     ylab = "Relative error", xlab = "Nominal level", type = "l", ylim = c(-0.08, 0.5),
     cex.lab = 1, col = "cornflowerblue")
abline(h = 0, col = "grey")
x <- sort(res_small_nonch$skovgaard1)
x <- x[index]
lines(ppoints(x), (x - ppoints(x))/ppoints(x),
      col = "seagreen3", lty = "dashed", lwd = 1.5)
x <- sort(res_small_nonch$skovgaard2)
x <- x[index]
lines(ppoints(x), (x - ppoints(x))/ppoints(x), lwd = 1.5,
      col = "seagreen4", lty = "longdash")

```



3 Applications

This section provides the R code that reproduces the outputs of Section 6 in the paper. The functions to be used in order to run the following analyses can be found in the script `simulation_functions.R` in the archive.

3.1 Cow data

The code chunk below loads the file `cowdata.txt` (Kenward 1987) from the archive and reproduces the numerical results regarding the veterinary trial on cattle reported in the main text.

```

setwd(res_dir)
source("simulation_functions.R")

##
## Attaching package: 'plyr'
## The following object is masked from 'package:graph':
##
##      join
## Loading required package: foreach
## Loading required package: iterators
## Loading required package: parallel
cow <- read.table("cowdata.txt", skip = 7, header = TRUE)

names(cow)[- (1:2)] <- paste("T", 1:11, sep = '')
cow.times <- cow[, - (1:2)]
cow.timesA <- cow[cow$G == "A", - (1:2)]
cow.timesB <- cow[cow$G == "B", - (1:2)]

## group A
cowsA <- cow.timesA
S <- cov(cowsA)
n <- nrow(cowsA)

# unsaturated model under H1
# MD(3)
G1 <- UG(~ T1*T2*T3*T4 + T2*T3*T4*T5 + T3*T4*T5*T6 + T4*T5*T6*T7 + T5*T6*T7*T8 +
          T6*T7*T8*T9 + T7*T8*T9*T10 + T8*T9*T10*T11)
model1 <- fitConGraph(G1, S, n)

# model under H0
# MD(1)
G0 <- UG(~ T1*T2 + T2*T3 + T3*T4 + T4*T5 + T5*T6 + T6*T7 + T7*T8 + T8*T9 + T9*T10 +
          T10*T11)

model0 <- fitConGraph(G0, S, n)

### tests
## w
lrt(model0, model1, n)

## $Woss
## [1] 28.38429
##
## $pvalue
## [1] 0.04064335

## w* and w**
Wstar(model0, model1, n, G1 = G1)

## $wstar1
##           [,1]
## [1,] 22.97676

```

```

##
## $p.value1
##           [,1]
## [1,] 0.1500088
##
## $wstar2
##           [,1]
## [1,] 22.6913
##
## $p.value2
##           [,1]
## [1,] 0.1595728
## directional p-value
dir_p(model0, model1, n , G1 = G1)$pvalue

## [1] 0.1113944
## group B
cowsB <- cow.timesB
S <- cov(cowsB)
n <- nrow(cowsB)

# unsaturated model under H1
# MD(3)
G1 <- UG(~ T1*T2*T3*T4 + T2*T3*T4*T5 + T3*T4*T5*T6 + T4*T5*T6*T7 + T5*T6*T7*T8 +
          T6*T7*T8*T9 + T7*T8*T9*T10 + T8*T9*T10*T11)
model1 <- fitConGraph(G1, S, n)

# model under H0
# MD(1)
G0 <- UG(~ T1*T2 + T2*T3 + T3*T4 + T4*T5 + T5*T6 + T6*T7 + T7*T8 + T8*T9 + T9*T10 +
          T10*T11)

model0 <- fitConGraph(G0, S, n)

### tests
## w
lrt(model0, model1, n)

## $Woss
## [1] 31.89548
##
## $pvalue
## [1] 0.01550424
## w* and w**
Wstar(model0, model1, n, G1 = G1)

## $wstar1
##           [,1]
## [1,] 30.05542
##
## $p.value1
##           [,1]
## [1,] 0.02594814

```

```
##
## $wstar2
##      [,1]
## [1,] 30.02809
##
## $p.value2
##      [,1]
## [1,] 0.02614321
## directional p-value
dir_p(model0, model1, n, G1 = G1)$pvalue

## [1] 0.02887994
```

3.2 Leukemia data

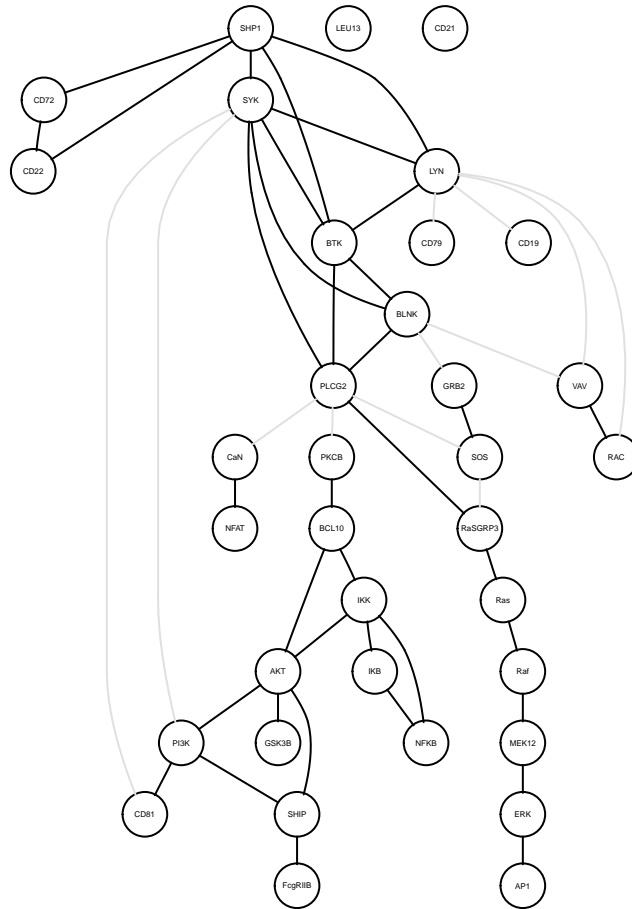
The next code chunks load from the archive the file `BCRdata.rda`, also accessible via the R package `topologyGSA` (Massa and Sales 2016), and reproduces Figure 7 and the numerical results regarding the genetic study on lymphocytic leukemia reported in the main text.

```
setwd(res_dir)
load("BCRdata.rda")

ug_bcell <- moralize(dag_bcell)
defAttrs <- getDefaultAttrs()
eAttrs <- list()
eAttrs$color <- c("SYK~PI3K" = "gray88", "SYK~CD81" = "gray88", "LYN~CD79" = "gray88",
  "LYN~CD19" = "gray88", "LYN~VAV" = "gray88", "LYN~RAC" = "gray88",
  "BLNK~VAV" = "gray88", "BLNK~GRB2" = "gray88", "PLCG2~CaN" = "gray88",
  "PLCG2~PKCB" = "gray88", "PLCG2~SOS" = "gray88",
  "SOS~RaSGRP3" = "gray88")

eAttrs$style <- c("SYK~PI3K" = "dotted", "SYK~CD81" = "dotted", "LYN~CD79" = "dotted",
  "LYN~CD19" = "dotted", "LYN~VAV" = "dotted", "LYN~RAC" = "dotted",
  "BLNK~VAV" = "dotted", "BLNK~GRB2" = "dotted", "PLCG2~CaN" = "dotted",
  "PLCG2~PKCB" = "dotted", "PLCG2~SOS" = "dotted",
  "SOS~RaSGRP3" = "dotted")

plot(ug_bcell, edgeAttrs = eAttrs, attrs = list(node = list(fontsize = "13")))
```



```
G1 <- as(ug_bcell,"matrix")

n <- nrow(y2)
S <- cov(y2)

# H1: unsaturated model
model1 <- fitConGraph(G1, S, n)

# H0: simpler BCR signaling pathway
G0 <- G1
G0["SYK", "PI3K"] <- G0["SYK", "CD81"] <- G0["PI3K", "SYK"] <-
  G0["CD81", "SYK"] <- 0
G0["LYN", "CD79"] <- G0["LYN", "CD19"] <- G0["LYN", "VAV"] <- G0["LYN", "RAC"] <-
  G0["CD79", "LYN"] <- G0["CD19", "LYN"] <- G0["VAV", "LYN"] <-
  G0["RAC", "LYN"] <- 0
G0["BLNK", "VAV"] <- G0["BLNK", "GRB2"] <- G0["VAV", "BLNK"] <-
  G0["GRB2", "BLNK"] <- 0
G0["PLCG2", "CaN"] <- G0["PLCG2", "PKCB"] <- G0["PLCG2", "SOS"] <-
  G0["CaN", "PLCG2"] <- G0["PKCB", "PLCG2"] <- G0["SOS", "PLCG2"] <- 0
G0["RaSGRP3", "SOS"] <- G0["SOS", "RaSGRP3"] <- 0

model0 <- fitConGraph(G0, S, n)

## w
lrt(model0, model1, n)
```

```

## $Woss
## [1] 33.51951
##
## $pvalue
## [1] 0.0008027688
## w* and w**
Wstar(model0, model1, n, G1 = G1)

## $wstar1
##           [,1]
## [1,] 32.17165
##
## $p.value1
##           [,1]
## [1,] 0.001301832
##
## $wstar2
##           [,1]
## [1,] 32.15782
##
## $p.value2
##           [,1]
## [1,] 0.001308256
## directional p-value
dir_p(model0, model1, n, G1 = G1)$pvalue

## [1] 0.001394133

```

References

- Kenward, Michael G. 1987. "A Method for Comparing Profiles of Repeated Measurements." *J. R. Statist. Soc. C* 36: 296–308.
- Massa, Sofia, and Gabriele Sales. 2016. *topologyGSA: Gene Set Analysis Exploiting Pathway Topology*. <https://CRAN.R-project.org/package=topologyGSA>.
- R Core Team. 2020. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing. <https://www.R-project.org/>.